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(54) Title: DISSOLUTION DYNAMIC NUCLEAR USING MATERIALS OBTAINED BY INCORPORATION OF RADICALS BY COVALENT BONDING ON EXISTING POROUS SOLIDS

(57) Abstract: The present invention concerns a process for polarizing ^{1}H, ^{13}C, ^{15}N or another nucleus of an analyte by dissolution dynamic nuclear polarization (D- DNP), said process comprising the successive steps of: i) providing a liquid sample containing the analyte to be polarized; ii) impregnating a porous material carrying radicals with the liquid sample containing the analyte, iii) cooling the impregnated material, at a temperature in the range from 0.5 K to 300 K, iv) submitting the impregnated material in the cooled state obtained in step, iii) to D-DNP conditions to polarize, directly or indirectly, the selected nuclear spin of the analyte, v) warming the impregnated material obtained after step iv) and passing a solution through the material which will carry the polarized analyte with it, wherein the material carrying radicals which is impregnated in step ii) was obtained by incorporating radicals through covaient bonding on an initial existing porous solid, this initial existing porous solid being exclusively inorganic or being a carbon based solid with a content of carbon representing at least 97% of the mass of the initial existing porous solid.

DISSOLUTION DYNAMIC NUCLEAR USING MATERIALS OBTAINED BY INCORPORATION OF RADICALS BY COVALENT BONDING ON EXISTING POROUS SOLIDS

This invention relates to the field of dynamic nuclear polarization (DNP) and concerns, in particular, Dissolution dynamic nuclear polarization (D-DNP). The present invention concerns the use materials which incorporate persistent radicals that are covalently linked to a porous solid and methods of dissolution DNP, which use such materials.

The technique of dynamic nuclear polarization (DNP) has been used to increase the nuclear magnetic polarization of samples, and thereby increases the sensitivity in Nuclear Magnetic Resonance (NMR) spectroscopy experiments, in particular, Metabolic Magnetic Resonance Imaging (metabolic MRI) and Magnetic Resonance Spectroscopy (MRS). For instance, DNP can be used to enhance the intensity of NMR signals, since NMR signals arise from transitions between nuclear spin states which have a very low energy difference and which are, thus, very weakly polarized at room temperature, leading to weak signals.

DNP refers to methods where the electron spin polarization is transferred to nuclear spins by the application of a resonant microwave excitation of the electronic spin transitions, and have applications in NMR or MRI/MRS (Golman et al. *PNAS* July 25, **2006**, vol. 103 n°30, 11270-11275).

The technique relies on the presence of unpaired electrons, which are more highly polarized in a magnetic field than nuclei owing to the much larger gyromagnetic ratio of the electron compared with nuclei. Unpaired electrons may thus be roughly 660 times more polarized than proton spins and 2600 times more polarized than carbon under the same conditions, i.e. in the same magnetic field and at the same sample temperature. DNP is the method whereby electron polarization is transferred to nuclei. This polarization can be transferred to the nuclei of the sample when the microwave irradiation is sufficient to induce transitions between the combined electron and nuclear magnetic energy levels of the polarizing agent.

Currently, two main approaches can be applied to obtain highly polarized nuclear spins in solution by DNP.

Overhauser induced DNP (« ODNP ») is an established technique with the first experiments dating back to six decades (Overhauser, 1953). Solutions that contain a polarizing agent with unpaired electrons (a radical) can be directly hyperpolarized by this approach. This effect is however limited to low magnetic fields, typically 0.35 T (above 1 T, the modulation of the electron-nuclei dipolar couplings is not efficient for magnetization transfer by the Overhauser effect). It has been shown by Griffin and coworkers (G. J. Gerfen et al. *J. Chem. Phys.* **1995**, *102*, 9494; L.*R. Becerra Phys. Rev. Lett.*, 71 (**1993**) 3561-3564 and D. A. Hall et al. *Science* **1997**, *276*, 930) that, at higher magnetic field and in particular cases where a coupling is established between the electron and a nucleus, the modulation of this through-bond interaction can give rise to a Overhauser effect and to significant NMR signal amplification.

J. H. Ardenkjær-Larsen et al developed a more recent approach (J. H. Ardenkjær-Larsen et al, *PNAS*, **2003**, 100, 10158-10163), in which the polarization of the nuclear spins is performed at low temperature in the solid-state. The sample is then rapidly dissolved to obtain a solution in which the nuclear spins of the molecules of interest are strongly polarized. This technique is referred to as Dissolution DNP (D-DNP). The increase of sensitivity was achieved by the use of a polarizing agent containing unpaired electron(s) with a doublet electronic state. The polarizing agent was dissolved in a solution containing the substance to be analyzed, and the solution cooled to 4.2 Kelvin or less in a polarizing magnetic field of 3.35 Tesla. The cold solution was irradiated with radio frequency radiation at the Larmor frequency of the electron (94 GHz). Then, the sample was warmed by the addition of room temperature solvent, and the spectra obtained within a few seconds after addition of the solvent. The irradiation step transferred the high polarization of the unpaired electron of the free radical to the nuclei of the sample and the hyper polarization was retained for several tens of seconds while the sample was warmed and dissolved in the diluting solvent. The dissolution experiment is usually performed in an *ex situ* DNP polarizer, consisting in a magnet, a cryostat to cool down the sample to a temperature often as low as 1.2 K and a microwave source. After polarization by microwave irradiation and rapid dissolution, the hyperpolarized liquid sample is

transferred to a high-resolution NMR spectrometer, where the NMR signal is detected. The NMR signals can be amplified by factors larger than 10 000. The radicals used to obtain the polarization can either be neutralized chemically or filtered out of solution. This method has mostly been used for nuclei with low gyromagnetic ratios (^{13}C and ^{15}N) and the detection of hyper-polarized protons using dissolution DNP remains challenging due to the shorter nuclear relaxation times. Single scan methods have been applied to obtain multi-dimensional correlation spectra.

Dissolution dynamic nuclear polarization (D-DNP) usually requires freezing molecules of interest, such as metabolites, at very low temperatures (generally 1,2 K < T < 1,5 K is used for polarization of ^{13}C, ^{15}N, ^{129}Xe, ^{89}Y, etc., but T can be increased up to 5K, and thus, can be comprised, for example, between 1K and 5 K) in a glassy matrix to obtain an homogeneous distribution of radicals and molecules of interest. At these temperatures, their nuclear spin polarization can be enhanced by up to 4-5 orders of magnitude when compared to room temperature. Such enhancements are achieved by saturating the electron spin resonance (ESR) transitions of persistent free radicals referred as polarizing agents (PAs) which must be added to the sample. D-DNP is followed by rapid dissolution (or melting) of the frozen sample with a burst of superheated solvent to give highly polarized solutions. Applications include the detection of intermediates in chemical reactions, protein folding in real time, or the detection of cancer by monitoring abnormal rates of metabolic reactions in humans.

In contrast to the great number of metabolite resonances in a small chemical shift range (ca. 10 ppm) resulting in difficult interpretation of ^{1}H spectra, peaks corresponding to ^{13}C metabolites of interest occur over a much larger range, approximately 200 ppm. However, ^{13}C applications *in vivo* have been limited by both nuclear features and the low concentrations of interrogated metabolites. The natural abundance of ^{13}C is indeed only 1.1%. In addition, the gyromagnetic ratio (g) of ^{13}C is only ¼ the g of ^{1}H, which further limits sensitivity. Finally, in contrast to water (60–70% of the human body), in which the concentration of ^{1}H is approximately 110 M, the most concentrated metabolites (for example, ascorbate and lactate) are present in the mM range *in*

vivo. Accordingly, Magnetic Resonance Imagery/Magnetic Resonance Spectroscopy (MRI/MRS) of endogenous ^{13}C is not possible within reasonable imaging times.

The development of rapid dissolution DNP methods has previously facilitated impossible *in vitro* and *in vivo* study of small molecules. Indeed, using D-DNP (Dissolution DNP), a solution of ^{13}C enriched metabolites is hyperpolarized and can be injected into a patient within a short time span to limit the loss of polarization. The DNP technique is generalizable to a large number of analytes, in contrast to other hyperpolarization methods such as spin-exchange optical pumping, parahydrogen induced polarization (PHIP) coupled with signal amplification by reversible exchange (SABRE).

Many ^{13}C substrates have been polarized using the DNP technique, but only a handful have been used so far for detailed *in vivo* studies, during which metabolites are not only detected but also localized to an organ/tissue of interest. To reach those results, large ^{13}C metabolite signals and chemical shift imaging [CSI] methods were used to separate the signals into voxels ("volume pixels"). Hyperpolarized [1-^{13}C] pyruvate,[1,4-$^{13}C_2$] fumarate, ^{13}C HCO_3, [1-^{13}C]acetate and [^{13}C,^{15}N]urea are examples of endogenous substances that can be considered as analytes, used to follow basic biochemistry with many potential applications in oncologic imaging (Nelson S. J. et al. *Science Translational Medicine* **2013**, 5 198; patent WO2009077575 ; Gallagher A. F. et al. *PNAS*, **2009**, 106, 19801; Gallagher F. A. et al. *Nature*, **2008**, 453, 940), imaging of heart (Flori A. et al., *Contrast Media & Molecular Imaging*, 2015, 10, 194-202) and imaging physiologic perfusion (von Morze C. et al., *Journal of magnetic resonance imaging: JMRI*, 2011, 33, 692-697). The DNP analytes may also be non-endogenous and include [2-13C] benzoylformic acid and [^{13}C,D3]-p-anisidine (used to detect reactive oxygen species), and salicylic acid (used to detect hydrophobic binding *in vitro*) (Lippert A. R. et al. *J. Am. Chem. Soc.*, **2011**, 133, 3776; H. Nonaka H. at al. *Nat. Commun.*, **2013**, 4, 2411; M. H. Lerche M. H. at al., *J. Magn. Reson.*, **2010**, 203, 52–56.).

These techniques have the potential to revolutionize the way patients are diagnosed and treated in clinic, *via* non-invasive insights into basic metabolism.

PAs with narrow EPR lines, such as Trityl radicals, are often used for the direct polarization of ^{13}C nuclei. In practice, polarizations P(^{13}C) of 20% or higher can be obtained after dissolution. It has recently been demonstrated that DNP of ^{13}C can be significantly accelerated by combining increased magnetic fields with polarization of ^{1}H rather than ^{13}C (using nitroxyl radicals such as TEMPO with broader ESR lines than Trityl radicals), followed by Hartmann-Hahn $^{1}H \rightarrow ^{13}C$ cross-polarization (CP) to transfer the polarization from ^{1}H to ^{13}C (Jannin S. et al. Chem. *Phys. Lett.* **2011**, 517, 234; Bornet A. et al. *Appl. Magn. Reson.* **2012**, 43, 107; Jannin S. et al. Chemical Physics Letters 2012, 549, 99; Bornet A. et al. *Journal of Physical Chemistry Letters* **2013**, 4, 111; Batel M. et al. *Chemical Physics Letters* **2012**, 554, 72, and WO 2013/153101A1). The final P(^{13}C) obtained is, thus, proportional to the ^{1}H polarization. The same authors have introduced in A. Bornet et al., Chemical Physics Letters, 602 (2014) 63-67, the concept of modulating the microwave frequency, instead of using a monochromatic frequency, for D-DNP application. The use of this frequency modulation increases the polarization P(^{1}H) and decreases the build-up time of glassy polarizing matrixes having low radical concentration. Indeed, the more diluted and the less homogeneously distributed are the radicals, the more the frequency modulation has an effect on the polarization.

Dissolution dynamic nuclear polarization (D-DNP) usually requires freezing molecules of interest at very low temperatures (1-5 K) in a glassy matrix to obtain a homogeneous distribution of molecules of interest and radicals. Typically, the radical is dissolved either in the liquid form of the molecule of interest (pure: [1-^{13}C]-Pyruvic acid) or in a solution containing the molecule of interest, a solvent and a glassy agent (such as glycerol, ethanol or DMSO) to prevent crystallization, i.e. phase segregation/inhomogeneity. This approach presents several drawbacks which are the limited number of analytes that can be polarized without the use of an anti-freeze (so far, only pyruvic acid). In addition, the presence of radicals in the solution is detrimental to both the polarization of the tracer (a radical is paramagnetic and fastens spin relaxation) and patient health. These agents are generally eliminated by precipitation followed by filtration or by solvent extraction, but the methods are substrate specific,

performed after the dissolution step, typically resulting in polarization loss.

In order to easily separate the polarizing agent (i.e. the radical) from the hyperpolarized solution, other authors described the use of radicals on solid supports to (hyper)polarize solutions and flowing fluids by DNP. Dorn et al., in *J. Am. Chem. Soc.* 110, 2294 (**1988**); *Anal. Chem.* 70, 2623-2628 (**1998**) have studied the polarization of several flowing organic solvents by ODNP using TEMPO immobilized on polymer beads and silica gel. This approach is dubbed SLIT DNP for flow Solid-Liquid Intermolecular Transfer DNP. The advantage of this approach is that a radical-free hyperpolarized solution is obtained. In favorable cases, ^{13}C (scalar-dominated) enhancements of 1-2 orders of magnitude could be obtained (for example, in mixtures of benzene and several chlorocarbons which were continuously "recycled" through the DNP spectrometer). This approach is however not general (i.e. is limited to cases where a transient coupling with the radical occurs) and a complex apparatus is needed.

An agarose gel containing covalently bound radicals (TEMPO) has been developed by S. Han et al. (*JMR*, **2008**, 190, 307–315) to polarize aqueous solutions (stagnant or in continuous flow) by ODNP, at room temperature and low magnetic field (0.35 T). The mobility of the radicals in the gel is sufficient for efficient polarization transfer via the Overhauser effect, without the radicals being released into the solution. However, as the radicals are immobilized and the mobility of the solution is reduced within the gel, the proton enhancements observed for the water signal are lower than those obtained when TEMPO is directly dissolved in the sample. This method has been limited so far to the enhancement of the water NMR signal.

In both techniques developed by Dorn et al. and Hans et al., the solution is polarized at low field and high temperature (>273K) before being subsequently transported into a high-resolution magnet. Therefore, these approaches are *ex-situ* polarization techniques. The methods have not been demonstrated yet as a general approach to detect small concentrations of substrates in solutions.

Ciriminna et al. (R. Ciriminna et al., Chemical Communications, (2000) 1441-1442 ; A. Michaud et al., Org. Process Res. Dev., 11 (2007) 766-768)

developed a non-structured TEMPO-rich material obtained by co-condensation as a catalyst for the selective oxidation of alcohols using NaOCl. This non-structured material, commercialized as SiliaCAT® (US 6,797,773 - Catalytic materials for selective oxidation of alcohols, process for production thereof and their use in alcohol oxidation process), was later used by Thankamony et al (A.S.L. Thankamony et al, Appl Magn Reson (2012) 43:237–250) for MAS-DNP application at 100 K, $NO^{\bullet}$ concentration used were 173 µmol/g. The sample did not contain any other component, and the notion of polarizing a substrate or an analyte of interest with such a material is not considered. Similar material obtained using similar route with a TEMPO concentration of 470 µmol/g was used for MAS-DNP at 100K by Gajan et al. (D. Gajan et al., Journal of the American Chemical Society, 135 (2013) 15459-15466). In both cases, the signal enhancement of the solvent or of the silicon of the support is very limited ($\varepsilon_H < 4$, $\varepsilon_{Si} \approx 1$).

A lot of non-structured materials comprising TEMPO groups are also used as catalytic materials for selective oxidation of alcohols (US 6,797,773). Indeed, literature is rich in examples of TEMPO-rich solids preparation for catalysis application, either using direct synthesis co-gel or surface grafting. The latter is full of examples which can be regrouped in two main categories: 1. the functionalization of a solid is carried through the reaction of the surface function followed by the reaction of this function with a TEMPO-containing reactant [A. Schatz, Chem. Eur. J. 2008, 14, 8262 – 8266; D. Brunel et al., Applied Catalysis A: General 213 (2001) 73–82; Fey T et al, J.Chem., Vol. 66, No. 24, '2001) 8154]; 2. TEMPO-containing reactant is directly reacted with a solid surface functions [Machado A, MICROPOR MESOPOR MAT, 203 (2015) 63; I. Kiricsi et al, Studies in Surface Science and Catalysis, Vol. 125].

The first method typically ends up with a high variety and complexity of surface species, while the two methods are typically applied to fully cover a solid surface for catalysis applications.

Noda, Yohei et al., in NUCL INSTRUM METH A 776 (2015) 8 developed a thermosetting polymer for dynamic nuclear polarization by solidification of an epoxy resin mixture including TEMPO. They performed DNP experiments of the

epoxy at 4.2 and 1.2 K and reached ^{1}H polarization as high as 35 %. It should be noted that only the obtained epoxy resin was polarized, the solid having low pore volume, barely any analyte can be impregnated in it.

Some of the inventors have previously proposed in WO 2014/023659, a material formed by a porous and structured network, this network being at least in part formed by Si atoms, or Si atoms and metal atoms, linked to each other by oxy bridges, characterized in that the material comprises organic molecules which include at least one radical and which are covalently bonded to the network *via* siloxy bonds. The amount of radicals is ranging from 0.03 to 0.50 mmol of radical per gram of material, and the network is formed with one sol-gel step using an organosilane for the introduction of the organic molecules allowing their regular distribution within the porous structured material. This material is particularly suitable as a polarizing agent for the signal enhancement of analytes in frozen solutions at low temperature (ca. 100K) using solid-state NMR techniques (i.e. MAS DNP); polarization being mainly induced by the cross effect mechanism.

D. Gajan et al., PNAS, October 14, 2014, vol. 111, n°41, 14693-14697 presents as well high performance in dissolution DNP (D-DNP) of structured material, due at least in part to the thermal mixing mechanism, with polarization occurring at temperatures below 5 K. The particular structure of the hyperpolarizing solids makes possible the polarization of any analyte dissolved in an aqueous solution without glassy agent such as glycerol or DMSO. In addition, the solution can efficiently and quickly be filtered out from any contaminants, that is from the polarizing solid and its PA. In addition, any persistent radical (trityl, TEMPO...) can be attached in theory to the surface of the structured material described, allowing both direct ^{13}C polarization and $^{1}H=>^{13}C$ Cross Polarization (CP) [Bornet et al., J. Phys. Chem. Lett., 4 (2013) 111]. The first generation of material described in D. Gajan et al., PNAS, October 14, 2014, vol. 111, n°41, 14693-14697 allowed one to produce [1-^{13}C]-pyruvate having a ^{13}C polarization of more than 25% after 11s long dissolution step, the polarization lasting 20-30 minutes using TEMPO radical and Cross-Polarization.

The main drawback of such hybrid organic-inorganic materials is that it is

typically present as a fine powder. This affects the filtration time and leads to a significant pressure drop problematic for D-DNP that requires a fast filtration with high pressure and overheated water. In addition, very fine powder (<100nm) are difficult to filter off the solution. The preparation of bulk solids, i.e. monolith or highly porous gel with hierarchical porous structure, is possible for inorganic structured materials but remains a challenge for inorganic-organic hybrid materials with homogeneous distribution of organic moieties.

The objective of the invention is to propose the use of a solid-phase polarization-medium prepared by surface treatment of an existing solid for D-DNP application, in particular, for the polarization of a frozen analyte at temperature lower than 15 K. This invention concerns the use in D-DNP of solid-phase polarization-solids obtained by post-treatment of any existing solids, ordered mesoporous materials or not. This invention concerns the fastening of radicals at the accessible surface of a porous solid (so called surface treatment), and allows the use of any porous solids obtained by any synthesis procedure for the treatment leading to covalent bonds between the radicals and the surface of existing porous solid, and consequently provides access to a broad variety of physical features (pore size, distribution, shape), easily tunable.

The invention concerns a process for polarizing ^{1}H, ^{13}C, ^{15}N or another nucleus of an analyte by dissolution dynamic nuclear polarization (D-DNP), said process comprising the successive steps of:

i) providing a liquid sample containing the analyte to be polarized;

ii) impregnating a material carrying radicals with the liquid sample containing the analyte,

iii) cooling the impregnated material, at a temperature in the range from 0.5 K to 300 K,

iv) submitting the impregnated material in the cooled state obtained in step iii) to D-DNP conditions to polarize, directly or indirectly, the selected nuclear spin of the analyte,

v) warming the impregnated material obtained after step iv) and passing a solution through the material which will carry the polarized analyte with it,

wherein the material carrying radicals which is impregnated in step ii) was obtained by incorporating radicals through covalent bonding on an initial existing porous solid, this initial existing porous solid being exclusively inorganic or being a carbon based solid with a content of carbon representing at least 97% of the mass of the initial existing porous solid.

The incorporation of radicals by covalent bonds on the initial existing porous solid can be carried out by only one step or by several steps.

Those materials are used for D-DNP applications for the production, after the so-called "dissolution" step (step v)), of a solution of the polarized analyte. The material according to the invention can be used for direct polarization or CP-DNP (cross-polarization DNP) through proton.

According to a first embodiment, the incorporation of radicals in the material used in step ii) is carried by grafting on accessible reactive functions present on the initial existing porous solid of:

- either organic molecules including at least one radical,
- or organic molecules including a functionality allowing, in one or several additional step(s), the introduction of organic molecules which include at least one radical ; for instance, such a functionality is selected from halogen atoms and functional groups such as azide, amine, amide, imine, nitrosyl, carboxyl, ketone, aldehyde, phosphine, phosphate, phosphinite, sulfoxide, -NCO, -CN -OH, -SH, or ether.

For instance, the organic molecules including at least one radical are grafted on the accessible surface of the material by a connecting moiety corresponding or including **-L1-**, **-L2-** or **-L1-L2-**, defined from the material to the radical, with **L1** chosen among the following groups in their bivalent form: C_{1-20} alkyl, C_{1-20} alkenyl, C_{1-20} alkynyl, C_6-C_{24} aryl, C_7-C_{44} alkylaryl, C_7-C_{44} alkenylaryl, C_7-C_{44} alkynylaryl, the said groups being able to contain triazole and tetrazole units and being unsubstituted or substituted with one or more moieties selected from C_{1-10} alkoxy, C_{1-10} alkyl, C_{1-10} aryl, amido, imido, phosphido, nitrido, C_{1-10} alkenyl, C_{1-10} alkynyl, arene, phosphane, sulfonated phosphane, phosphate, phosphinite, arsine, ether, amine, amide, imine, sulfoxide, carboxyl, nitrosyl, pyridine, substituted pyridine, imidazole, substituted imidazole, triazole, tetrazole,

pyrazine, substituted pyrazine and thioether ; and **L2** chosen among –O-, -NH-, -N(C_{1-6} alkyl)-, -N(phenyl)-, -N(benzyl)-, -C(O)-, -C(O)O, -OC(O)-, -S-, -SO_2-, -N=N-, -NHC(O)- and -CONH-.

According to a second embodiment, the incorporation of radicals in the material used in step ii) is carried by a sol-gel step involving an organic moiety carrying at least one radical or carrying a functionality allowing, in one or several additional step(s), the introduction of the organic molecules which include at least one radical, leading to the formation of a layer on the accessible surface of the initial existing porous solid.

Advantageously, the layer is obtained by a sol-gel method involving at least two precursors:

- at least one tetraalkoxysilane, tetrahydroxysilane, alkoxymetal, hydroxymetal, alkoxyhydroxysilane, alkoxyhydroxymetal, silicate or metallate in which the metal is Zr, Ti or Al,

and at least one organosilane corresponding to a monosilyl or a polysilyl entity, for instance, chosen among the organotrialkoxysilanes, organotrichlorosilanes, organotris(methallyl)silanes, organotrihydrogenosilanes, di-organosilane such as diorganodialkoxy or dichlorosilane, or disilyl compounds of general formula X_3Si-R'-SiX_3 with X = halogen, alkoxy, hydroxyl, methallyl or hydrogen, R' being any organic moiety, with at least one of the selected organosilane carrying the organic molecule which includes at least one radical or carrying a functionality allowing, in one or several additional step(s), the introduction of the organic molecules which include at least one radical.

In particular, the layer is formed:

- either by Si atoms, or Si atoms and metal atoms, linked to each other by linking arms consisting in an oxy bridge and by organic linking arms, with at least some of these organic linking arms comprising one said organic molecule which includes at least one radical,
- or by Si atoms, or Si atoms and metal atoms, exclusively linked to each other by linking arms consisting in an oxy bridge and wherein the organic molecules which include at least one radical are covalently bonded to one Si atom of the layer.

Advantageously, the material used in step ii) has one of the following characteristics, a combination of the following characteristics or even all the following characteristics when they do not exclude one another:

- the amount of radicals in the material is in the range of 0.5 to 160 µmol per gram of material, preferentially in the range of 2 to 100 µmol per gram of material ;

- the material is non-structured or structured, preferably structured in a hexagonal array of the pores or in a cubic or worm-like arrangement of the pores;

- the total pore volume of the material ranges from 0.3 to 230 $cm^3.g^{-1}$, preferentially from 0.7 to 150 $cm^3.g^{-1}$,

- the mean pore diameter of the material belongs to the range from 2 nm to 10 µm, and preferably to the range from 3.5 nm to 2 µm, and preferentially from 3.5 to 500 nm ;

- the radicals are persistent radical preferably chosen among carbon-centered triarylmethyl radicals, nitronylnitroxides, nitroxides such as TEMPO, TEMPOL, azephenylenyls, verdasyls and Fremy's salt, and radicals chosen among perchlorophenylmethyl radical, tris(2,4,6-trichlorophenylmethyl radical), 1,3-bisdiphenylene-2-phenylallyl) and 2,2-diphenyl-1-picrylhydrazyl, galvinoxyl and their derivatives.

Description of the material used as source of electron in the D-DNP applications

The material carrying radicals which is impregnated in step ii) was obtained by incorporating radicals by covalent bonding on an initial existing porous solid. The initial existing porous solid will be described first and the incorporation of radicals within or on this material will be described afterwards.

Description of the initial existing porous solid

The material of the invention is porous and so includes pores and walls. It can be structured or non-structured. The initial existing solid has a porosity higher than the desired porosity of the final material obtained after the treatment used for the incorporation of radicals, and the two porosities should preferentially be close to each other. Its organization/structuration will determine the

organization/structuration of the material obtained after the treatment used for the incorporation of radicals.

The initial existing porous solid can exclusively be inorganic (it means that it does not include carbon) or can be a carbon based solid with a content of carbon representing at least 97% of the mass of the initial existing solid.

Preferred inorganic existing porous solid are formed by Si atoms, or Si atoms and metal atoms, or metal atoms, linked to each other by oxy bridges and correspond to inorganic oxides. Preferred examples of such inorganic existing solid are silica SiO_2, alumina Al_2O_3, TiO_2 and ZrO_2. Typical examples are silica gel, precipitated alumina/titania/zirconia, flamed silica/alumina/titania/zirconia, structured SBA-15 or MCM-41...

Carbon based porous solid with a content of carbon representing at least 97% of the mass of the initial existing porous solid are formed by carbon atoms directly linked to each other. Such a solid can be, for instance, carbon nanotubes, carbon nanofibers, carbon whiskers, charcoal or graphite.

Those materials are commercially available or can be prepared by available techniques, such as sol-gel or condensation/precipitation for inorganic solids and such as methane cracking for carbon-based solids. Those materials classically present accessible functions, typically –M–OH (with M being Si, Al, Ti or Zr, for instance) for inorganic oxides and –C=O, –C–OH and/or –COOH for carbon based solid. Those functions are called native functions as they are naturally found at their surface, i.e. ≡SiOH or ≡AlOH and ≡Al-OH-Al≡ are naturally found at the surface of pure silicon oxide and pure alumina, respectively. These functions are reactive functions which can be used for the introduction of the radicals on the initial existing porous solid. They will form covalent links, either directly with an organic molecule carrying at least one radical or with a layer used for the introduction of the radical, as explained hereafter.

Incorporation of radicals

The introduction of radicals with covalent links on the initial existing porous solid can be obtained by different ways, involving the reactive functions present on the initial existing porous solid. As preferred embodiments, a material used according to the invention is obtainable by a treatment involving the reaction of

the native functions which are present on the existing porous solid with one or several organic moiety with at least one of these organic moiety which carries at least one radical or a functionality allowing in one or several additional step(s), the introduction of the radicals.

According to a first embodiment, the introduction of the radicals is carried out by grafting, and in particular, by grafting on the accessible surface of the initial existing porous solid. The surface corresponds to the accessible surface of the initial existing porous solid, including the surface of the pores in its mass. To accessible surface is referred a surface that will be in direct contact with the used reactants when the solid is immersed or impregnated with a solution containing the reactants or exposed to reactants in gas phase.

The grafting is carried out on accessible reactive functions present on the initial existing porous solid using:

- either organic molecules including at least one radical,
- or organic molecules including a functionality allowing, in one or several additional step(s), the introduction of organic molecules which include at least one radical ; for instance, such a functionality is selected from halogen atoms and functional groups such as azide, amine, amide, imine, nitrosyl, carboxyl, ketone, aldehyde, phosphine, phosphate, phosphinite, sulfoxide, -NCO, -CN -OH, -SH, or ether.

The grafting method is preferentially achieved in conditions allowing a slow reaction between the surface and the organic moiety to favor a homogeneous distribution throughout the surface. This can be done, for instance, by controlling, for a set reactant and surface, the temperature and reaction time.

The grafting results in the formation of at least one covalent link.

Such a grafting method may comprise the following step(s):

a) the reaction between an accessible reactive function of the initial existing porous solid and one or several organic moieties chosen among:

- an organosilane corresponding to a monosilyl or a polysilyl entity, for instance, chosen among the organotrialkoxysilanes, organotrichlorosilanes, organotris(methallyl)silanes, organotrihydrogenosilanes, di-organosilane such as diorganodialkoxy or dichlorosilane, or disilyl compounds, for instance of

general formula $(Xa)_3Si-R'-Si(Xa)_3$ with Xa = halogen, alkoxy, hydroxyl, methallyl or hydrogen, R' being any organic moiety, with at least one of the selected organosilane carrying the organic moiety which includes at least one radical or carrying a functionality allowing in one or several additional step(s), the introduction of the organic molecules which include at least one radical,

- an organic molecule carrying a function suitable for forming a covalent bond with the reactive functions present on the initial existing porous solid, preferentially for carbon-based solids, chosen among isocyanates, diazonium salts, OCN-, $-SOCl_2$, cyanuric trichloride, -COCl, alcohols, amines, carbodiimides and azido ;

b) when the step a) uses a trialkoxysilane or an organic molecule carrying a functionality, one or several additional step(s) are conducted for obtaining the covalent link between the functionality and organic molecules which include at least one radical on the solid.

According to one embodiment, for the functionalization of oxides or carbon-based solids surfaces, the step a) uses an organic or organosilane moiety carrying a functionality selected from halogen atoms and functional groups such as azide, amine, alkyne, alkene, amide, imine, nitrosyl, carboxyl, ketone, aldehyde, phosphine, phosphate, phosphinite, sulfoxide, -NCO, -CN -OH, -SH, and ether, preferentially azide, -NCO, -SH, amine, alkyne. More information can be found, for instance, in [S. Banerjee et al., Advanced Materials, 17 (2005) 17] or [A. Schätz et al., A European Journal, 14 (2008) 8262] for carbon surface functionalisation and in [S.A. McCarthy et al., Nat. Protocols, 7 (2012) 1677] for oxides. Examples of reactions between surface functionalities and molecule bearing a radical leading to covalent bonds between the solid surface and the organic molecule including one radical can be found in W. Xi et al., Advanced Functional Materials, 24 (2014) 2572.

Such grafting will, for instance, lead to covalent bonds between the existing porous solid and organic molecules carrying at least one radical or a functionality allowing in one or several additional step(s), the introduction of organic molecules which include at least one radical, *via* a connecting moiety

corresponding or including -**L1**-, -**L2**- or -**L1**-**L2**-, defined from the material to the radical, with **L1** chosen among the following groups in their bivalent forms: C_{1-20} alkyl, C_{1-20} alkenyl, C_{1-20} alkynyl, C_6-C_{24} aryl, C_7-C_{44} alkylaryl, C_7-C_{44} alkenylaryl, C_7-C_{44} alkynylaryl, the said groups being able to contain triazole and tetrazole units and being unsubstituted or substituted with one or more moieties selected from C_{1-10} alkoxy, C_{1-10} alkyl, C_{1-10} aryl, amido, imido, phosphido, nitrido, C_{1-10} alkenyl, C_{1-10} alkynyl, arene, phosphane, sulfonated phosphane, phosphate, phosphinite, arsine, ether, amine, amide, imine, sulfoxide, carboxyl, nitrosyl, pyridine, substituted pyridine, imidazole, substituted imidazole, triazole, tetrazole, pyrazine, substituted pyrazine and thioether ; and **L2** chosen among –O-, -NH-, -N(C_{1-6} alkyl)-, -N(phenyl)-, -N(benzyl)-, -C(O)-, -C(O)O, -OC(O)-, -S-, -SO_2-, -N=N-, -NHC(O)- and -CONH-.

According to a second embodiment, the incorporation of radicals in the material used in step ii) is carried by a sol-gel step involving an organic moiety carrying at least one radical or carrying a functionality allowing, in one or several additional step(s), the introduction of the organic molecules which include at least one radical, leading to the formation of a layer on at least a part of the accessible surface of the initial existing porous solid.

Whatever the process used, in particular grafting or sol-gel step for the introduction of radicals, it is possible to include one or several steps of functionalization of the initial existing porous solid being exclusively inorganic or being a carbon based solid with a content of carbon representing at least 97% of the mass of the initial existing porous solid. The introduced functionalization can be used for the introduction of the radicals or not. For instance, they can be implemented for another purpose, for instance for the modification of the properties of the material.

The sol-gel method will lead to the formation of a layer at the accessible surface of the solid, in particular from atomic thickness to micrometric thickness that will cover, at least in part the accessible surface of the existing porous solid. It should be noted that a layer may not completely cover the accessible surface of the existing porous solid: the amount of silicon precursor and metal precursor, if any, may not be sufficient to fully cover the surface with a monoatomic layer,

resulting in the random distribution of those precursors along the surface. During this sol-gel step, covalent links are made between the layer formed and the native reactive functions of the surface of the existing porous solid.

A "sol-gel process" is a wet-chemical technique for the fabrication of materials (typically a metal oxide) starting from a chemical solution that reacts to produce particles or films (Hench, Larry L., Chemical Reviews (Washington, DC, United States) (1990), 90(1), 33-72). Typical precursors are metal alkoxides and metal chlorides, which undergo hydrolysis and polycondensation reactions to form in the presence of high surface area solid a film at its surface, a film with varying thickness throughout the surface (size ranging from molecular size to micrometric size), along with some particles in suspension in the solvent. The sol progresses towards the formation of a layer of inorganic network containing a liquid phase (gel). Formation of a metal oxide involves connecting the metal centers with oxo (M-O-M) or hydroxo (M-OH-M) bridges, therefore, generating metal-oxo or metal-hydroxo polymers at the surface of the solid. The drying process serves to remove the liquid phase from the gel, thus, forming a layer, porous or not, and then, a thermal treatment (firing) may be performed in order to favor further polycondensation and enhance mechanical properties. It should be noted that the sol-gel can be performed under classic hydrolytic conditions, as well as non-hydrolytic conditions (absence of water during the preparation).

The classical sol-gel process and the synthesis of hybrid nanostructured materials by sol-gel process using a templating route have been respectively described by Corriu R.J.P et al. in Angew. Chem. Int; Ed. 1996, 35, 1420-1436 and in J. Mater. Chem 2005, 15, 4285. The formation of ca. 1nm thick layer of silicon-based layer can be found in C. H. Chu et al., Anal. Chem. 1993, 65, 808-816. We can also refer to Dossier Techniques de l'Ingénieur, j5820 "Procédé sol-gel de polymerization" by P. Audebert and Miomandre, available version in July 2012. We can, for instance, refer to Y.F. Lu et al., Nature, 389 (1997) 364-368 or to C. Sanchez et al., Chem. Mat., 20 (2008) 682-737 or to X.Y. Liu et al., Mater. Sci. Eng. R-Rep., 47 (2004) 49-121.

The layer may be formed:

- either by Si atoms, or Si atoms and metal atoms, linked to each other by linking arms formed only by an oxy bridge and by organic linking arms, with at least some of these organic linking arms comprising one said organic molecule which includes at least one radical,
- or by Si atoms, or Si atoms and metal atoms, exclusively linked to each other by linking arms formed only by an oxy bridge and wherein the organic molecules which include at least one radical are covalently bonded to the layer by one Si atom,
- or by Si atoms, or Si atoms and metal atoms, linked to each other by linking arms consisting in an oxy bridge and by organic linking arms, wherein the organic molecules which include at least one radical are covalently bonded to one Si atom of the layer.

According to preferred embodiments, the organic molecules including the radicals are covalently bonded to the layer by one Si atom. In another preferred embodiment, some Si atoms and/or metal atoms which constitute the layer of the material are linked to each other by the organic molecules which include at least one radical. In that case, the organic molecules which include at least one radical form a part of the layer, and can be linked to two or three Si or metal atoms of the layer.

Advantageously, the layer or its inorganic part is made of silica SiO_2, alumina Al_2O_3, TiO_2 or ZrO_2.

As preferred embodiments, the layer is, at least in part, formed by Si atoms or both by Si atoms and metal atoms, linked to each other by oxy bridges and with the organic molecules which include at least one radical being covalently bonded to the layer by one Si atom or forming a part of the layer, and is obtainable by:

a) a sol-gel step involving at least two precursors:

- at least one tetraalkoxysilane, tetrahydroxysilane, alkoxymetal, hydroxymetal, alkoxyhydroxysilane, alkoxyhydroxymetal, silicate or metallate in which the metal is, for instance, Zr, Ti or Al,
- and at least one organosilane corresponding to a monosilyl or a polysilyl entity, for instance, chosen among the organotrialkoxysilanes, organotrichlorosilanes, organotris(methallyl)silanes,

organotrihydrogenosilanes, di-organosilane such as diorganodialkoxy or dichlorosilane, or disilyl compounds, for instance, of general formula $(Xa)_3Si$-R'-$Si(Xa)_3$ with Xa = halogen, alkoxy, hydroxyl, methallyl or hydrogen, R' being any organic moiety, with at least one of the selected organosilane carrying the organic moiety which includes at least one radical or carrying a reactive function allowing, in one or several additional step(s), the introduction of the organic molecules which include at least one radical ;

b) when the step a) uses an organosilane carrying a reactive function, one or several additional step(s) are conducted for obtaining the covalent link of the organic molecules which include at least one radical on the inorganic network.

It should be noted that when the network of the layer is at least in part formed by Si atoms linked to each other by oxy bridges and linking arms consisting in organic molecules, only organosilanes may be used.

For instance, the organosilane used for the introduction of the organic molecule which includes at least one radical, is carrying a reactive function selected from halogen atoms and functional groups such as azide, amine, amide, imine, nitrosyl, carboxyl, ketone, aldehyde, phosphine, phosphate, phosphinite, sulfoxide, -NCO, -CN -OH, -SH, and ether. In a preferred embodiment, the materials according to the invention are obtained by Azide-alkyne Huisgen cycloaddition (AAC) for the introduction of the organic molecules which include at least one radical. So, in this case, the reactive function will be a function that can be directly used in an AAC reaction, which is an azide group $-N_3$ or an alkyne, or a function which can lead, preferably in a simple way, to such a function, for instance, an halogen atom (typically Cl), -OH, a carboxylic acid or $-NH_2$. In another embodiment, the step a) uses an organosilane carrying an azide function, which is further transformed in a NH_2 function, on which a reaction is carried with an organic molecule which includes at least one radical and a carboxyl group in order to form a NH-CO link.

In a particular embodiment, the layer is, at least in part, formed by Si atoms or both by Si atoms and metal atoms, linked to each other by oxy bridges and with the organic molecules which include at least one radical being

covalently bonded to the layer by one Si atom or forming a part of the layer, and is obtained by:

a) a sol-gel step involving at least three precursors:

- at least one tetraalkoxysilane, tetrahydroxysilane, alkoxymetal, hydroxymetal, alkoxyhydroxysilane, alkoxyhydroxymetal, silicate or metallate in which the metal is, for instance, Zr, Ti or Al,
- and at least two organosilanes corresponding to a monosilyl or a polysilyl entity, for instance, chosen among the organotrialkoxysilanes, organotrichlorosilanes, organotris(methallyl)silanes, organotrihydrogenosilanes, di-organosilane such as diorganodialkoxy or dichlorosilane, or disilyl compounds, for instance, of general formula $(Xa)_3Si$-R'-$Si(Xa)_3$ with Xa = halogen, alkoxy, hydroxyl, methallyl or hydrogen, R' being any organic moiety, with at least one of the selected organosilane carrying the organic moiety which includes at least one radical or carrying a reactive function allowing, in one or several additional step(s), the introduction of the organic molecules which include at least one radical ;

b) when the step a) uses an organosilane carrying a reactive function, one or several additional step(s) are conducted for obtaining the covalent link of the organic molecules which include at least one radical on the inorganic network.

According to this particular embodiment, the introduction of a second organosilane enables the tailoring of the properties of the obtained material. In particular, alkyl groups like methyl or aryl groups like phenyl can be introduced on the material.

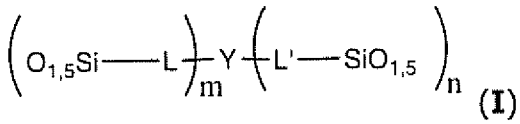
If desired, the sol-gel method is achieved in water with or without at least one co-solvent or in an appropriate polar solvent along with water. The sol-gel step will be carried out without a structure-directing agent for obtaining a non-structured layer or with a structure directing agent for obtaining a structured layer.

The amounts of the selected organosilane carrying the radical or a reactive function allowing in one or several additional step(s), the introduction of the organic molecules carrying the radical and the amount of reactants in the one or

several additional steps, will be chosen by the man skilled in the art for allowing the introduction of the desired concentration of radicals in the solid.

A further step can be included after the step a) or b) which consists in removing the residual hydroxyl or alkoxy groups. This is typically done by reaction of the material with passivating agents, typically considered as hydrophobic and chosen among trialkylsilyl derivatives (chloro, bromo, iodo, amido or alkoxysilanes) or alcohols.

Examples of layers comprise at least one organic-inorganic component (**I**), distributed within it, and of formula (**I**):



(**I**)

wherein:

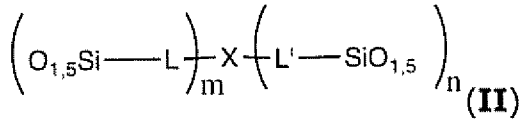
Y is a moiety, which includes at least one radical,

L and **L'** can be identical or different and are connecting organic moiety,

n and **m** can be identical or different and are integers selected as $1 \leq m+n < 5$,

the $SiO_{1,5}$ are part of the layer that is inorganic or hybrid inorganic-organic.

Such materials can also comprise at least one organic-inorganic component (**II**), distributed within it, and of formula (**II**):



(**II**)

wherein:

X is a moiety including at least one reactive function allowing in one or several additional step(s), the introduction of at least one radical,

L and **L'** can be identical or different and are connecting organic moiety,

n and **m** can be identical or different and are integers selected as $1 \leq m+n < 5$,

the $SiO_{1,5}$ are part of the inorganic part of the layer.

For clarifying the reading of formula (**I**) and (**II**), when **m**=2, for instance, it means that respectively **Y** or **X** are covalently bonded by two different covalent bonds to two –**L**-$SiO_{1,5}$ groups.

$SiO_{1,5}$ is used in order to indicate that the 3 Si-O bonds are shared between the inorganic-inorganic compound (**I**) (or (**II**)) and the inorganic layer, which is classically used by the man skilled in the art.

L and **L'**, identical or different, can be, for instance, hydrocarbonated connecting moiety which can be linear, branched or include a cycle which can be saturated or unsaturated, substituted or non-substituted, and which can include in its chain or cycle, one or several oxygen, sulfur or nitrogen heteroatom and/or one or several groups chosen among -CO-, -CONH-, -COO-, -NHCO-, -N=N-, -S(O)-, -$S(O)_2$-, -P(=O)(ORa)-, with Ra being a C_1-$_8$ alkyle.

For instance, **L** and **L'** can be identical or different, and defined from the Si atom to **Y** (or **X**) by the structure –**L1**-**L2**- in which **L1** is chosen among the following groups in their bivalent forms: C_{1-20} alkyl, C_{1-20} alkenyl, C_{1-20} alkynyl, C_6-C_{24} aryl, C_7-C_{44} alkylaryl, C_7-C_{44} alkenylaryl, C_7-C_{44} alkynylaryl, the said groups being able to contain triazole and tetrazole units and being unsubstituted or substituted with one or more moieties selected from C_{1-10} alkoxy, C_{1-10} alkyl, C_{1-10} aryl, amido, imido, phosphido, nitrido, C_{1-10} alkenyl, C_{1-10} alkynyl, arene, phosphane, sulfonated phosphane, phosphate, phosphinite, arsine, ether, amine, amide, imine, sulfoxide, carboxyl, nitrosyl, pyridine, substituted pyridine, imidazole, substituted imidazole, triazole, tetrazole, pyrazine, substituted pyrazine and thioether ; and **L2** is chosen among –O-, -NH-, -N(C_{1-6} alkyl)-, -N(benzyl)-, -N(phenyl)-, -C(O)-, -C(O)O-, -OC(O)-, -S-, -SO_2-, -N=N-, -NHC(O)- and -CONH-. For more details, see G. Parkin, Comprehensive Organometallic Chemistry III, Vol. 1, Chap. 1, Ed. Elsevier 2007.

X can be an azide group -N_3 or an alkyne, or a function which can lead, preferably in a simple way, to such a function, for instance, an halogen atom (typically Cl), -OH, a carboxylic acid or –NH_2.

The term used for the definition of the moieties have their usual meanings. In particular:

Alkyl is a saturated hydrocarbonated moiety which can be linear, branched or cyclic. Methyl, ethyl, cyclohexyl, ter-butyl are examples of alkyl.

Aryl is an unsaturated mono or polycyclic hydrocarbonated moiety which at least includes an aromatic cycle. Examples of aryl are phenyl and naphtyl groups.

Alrylalkyl is an unsaturated hydrocarbonated moiety which at least includes an aryl part and an alkyl part. Benzyl is an example of arylalkyl.

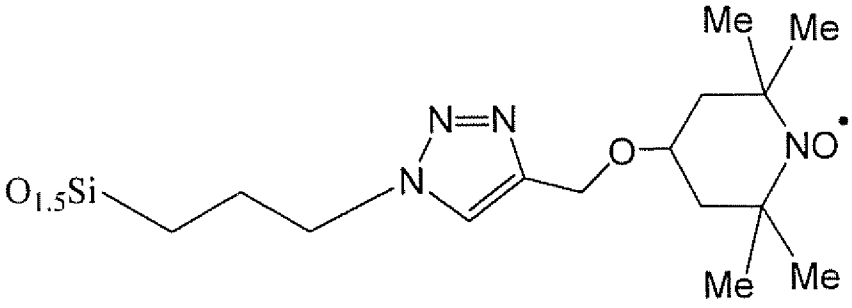
Alkenyl is an unsaturated hydrocarbonated moiety which can be linear, branched or cyclic and which at least includes one double bond.

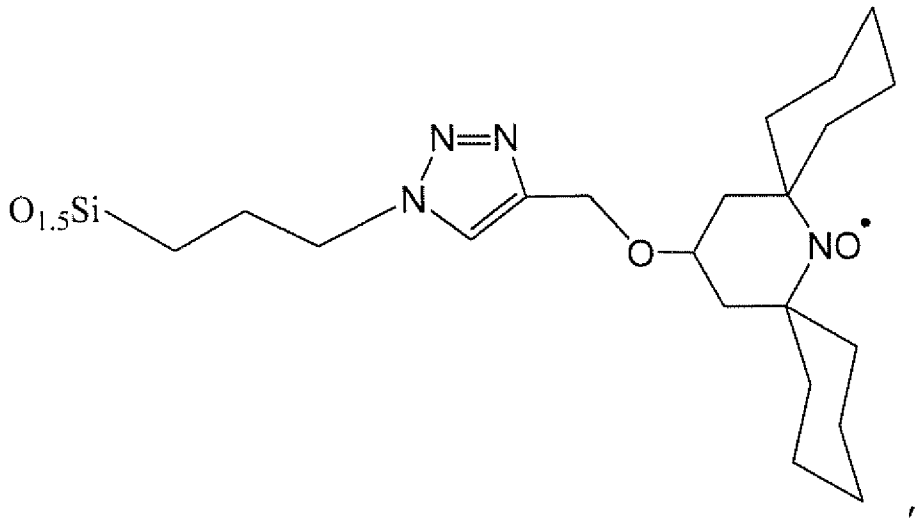
Alkynyl is an unsaturated hydrocarbonated moiety which can be linear, branched or cyclic and which at least includes one triple bond.

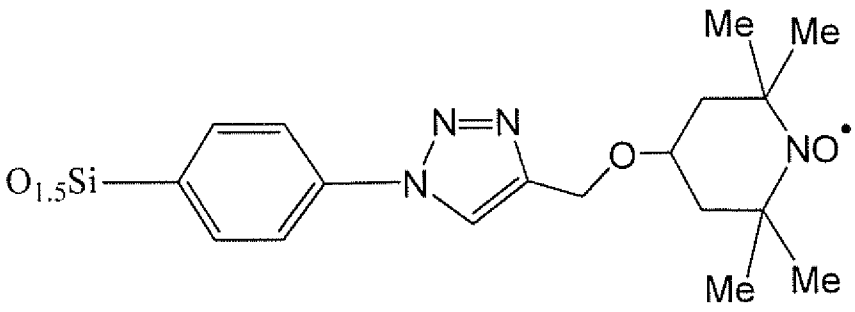
When, **m**=1 and **n**=0 and, the organoalkoxysilane is a monosilyl derivative and as a result, the organic molecules corresponding to **–L-X** will be located at the surface of the layer(i.e. in the pores).

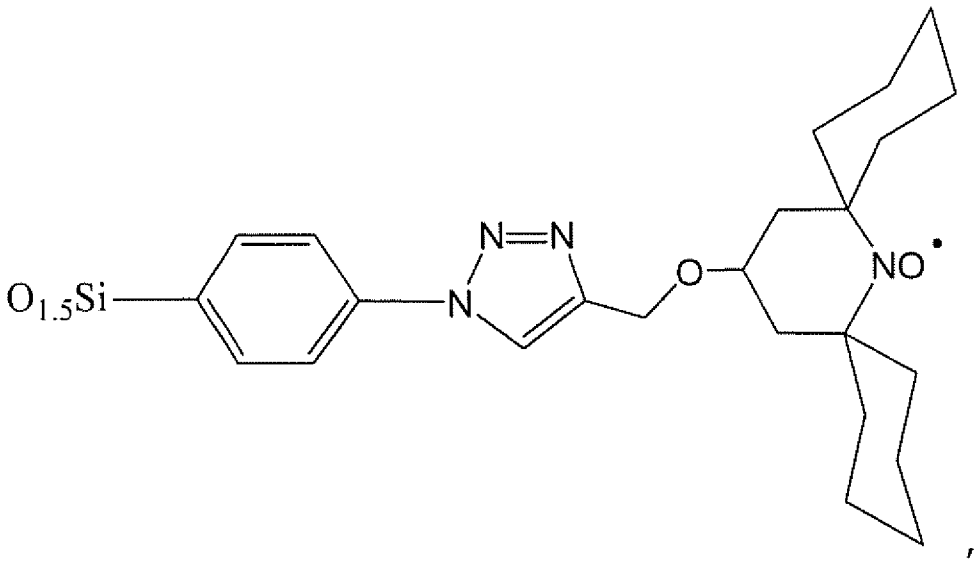
According to another embodiment, 2≤**m**+**n** and, the organoalkoxysilane is a polysilyl derivative (for instance, a bisilyl one) and as a result, the organic part corresponding to (**L**)**m**-**X**-(**L'**)**n** will located in the bulk of the layer (i.e. in the walls).

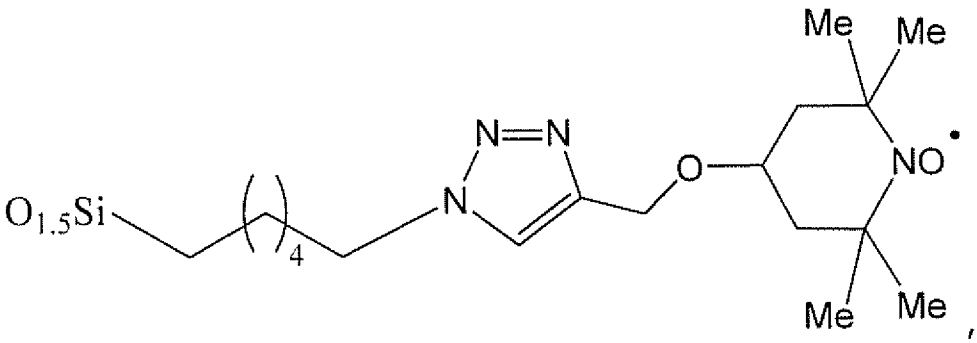
For instance, the organic-inorganic component (**I**) is chosen among:



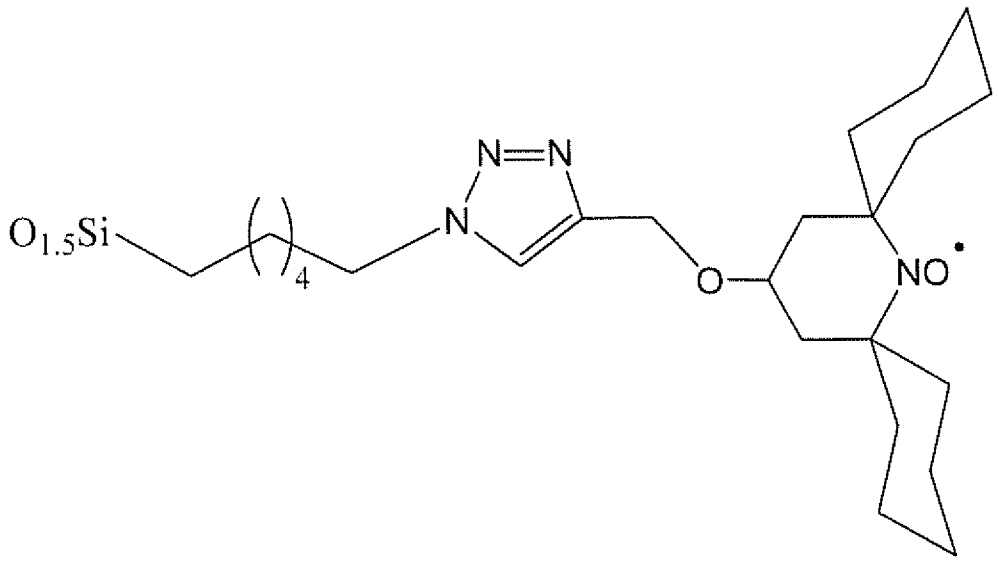




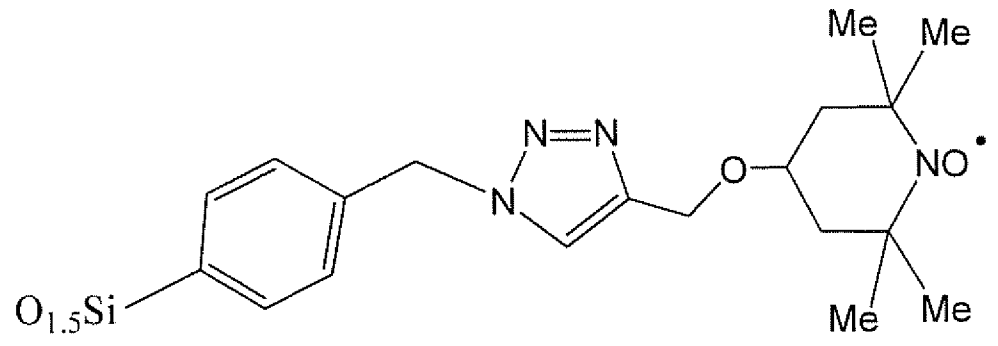



Me
Me
N=N
O
NO
$O_{1.5}Si$
4
N
Me
Me

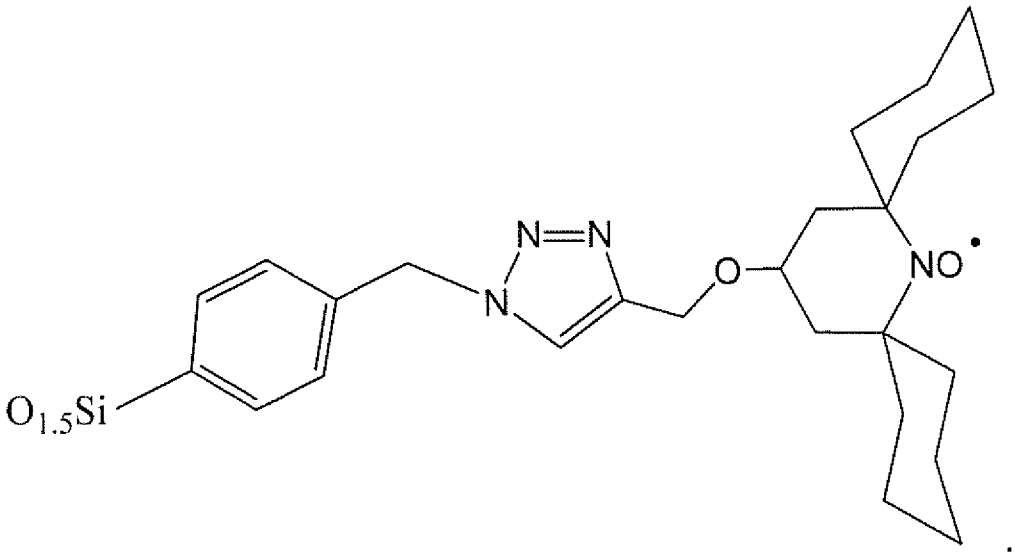
,


N=N
$O_{1.5}Si$
4
N
O
NO

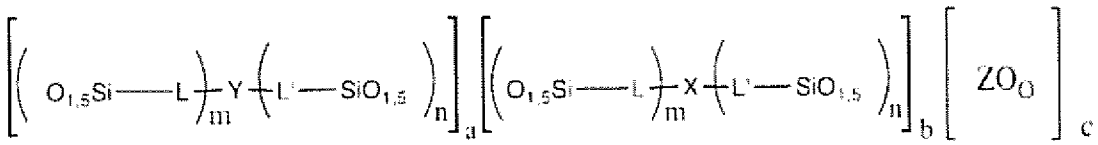
,


Me
Me
N=N
O
NO
$O_{1.5}Si$
N
Me
Me

and



An example of layer corresponds to a material of formula (**III**):



(**III**) wherein:

a, b and **c** can be identical or different and are integers selected as **a**>0, 0 ≤ **b**/**a** ≤1000 and 1 ≤ (**a**+**b**+**c**)/(**a**+**b**) ≤1000,

the **Z** atom is selected from silicon Si, zirconium Zr, titanium Ti, aluminium Al, and **o** is 2 when **Z** is Si, Zr or Ti and **o** is 1.5 when Z is Al

and **L**, **L'**, **X**, **Y**, **m** and **n** are as defined for formula (**I**).

Main characteristics of the material used in step ii) obtained after treatment and introduction of radicals

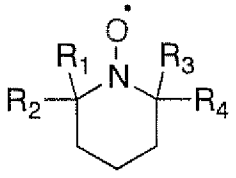
The organic molecules which at least include one radical are covalently bonded on the accessible surface of the material. Indeed, because the existing material treated is porous, the functionalization during the treatment of this existing material, for the introduction of the radicals (by grafting or by sol-gel), also occurred within the pores of the material. So, the accessible surface also includes the surface of the pores of the material localized in the mass of the material. The accessible surface includes any surface that will be exposed to the reactants during the functionalization step, i.e. the surface is at the outer part of

a particle or connected to it by pores large enough for said molecules to diffuse to it.

The materials used in the D-DNP according to the invention comprise organic molecules with unpaired electrons, named radicals in the present invention. These radicals will act as an electron source for DNP, and in particular, in dissolution DNP. So, the materials described in the invention are useful for Nuclear Magnetic Resonance spectroscopy, and more particularly, in MRI analysis through dissolution DNP.

The amount of radicals in the material is in the range of 0.5 to 160 µmol per gram of material, preferentially in the range of 2 to 100 µmol per gram of material.

Whatever the structure of the materials used in the D-DNP according to the invention, the radical(s) that is (are) present is (are) preferably (a) persistent radical(s). The radicals which are linked to the material are persistent, i.e. stable, due to steric crowding around the radical center, which makes it physically difficult for the radical to react with another molecule. Examples of such persistent radicals include carbon-centred triarylmethyl radicals (trityl), Fremy's salt (Potassium nitrosodisulfonate, $(KSO_3)_2NO^{\bullet}$), nitronylnitroxides, nitroxides ($NO^{\bullet}$ with N linked to two organic groups) such as TEMPO, TEMPOL, azephenylenyls and verdasyls, and radicals chosen among PTM (perchlorophenylmethyl radical), TTM (tris(2,4,6-trichlorophenylmethyl radical), BDPA (1,3-bisdiphenylene-2-phenylallyl) and DPPH (2,2-diphenyl-1-picrylhydrazyl), galvinoxyl and their derivatives. For instance, the organic molecule including the radical and, so the group **Y** in formula (**I**), can be a cyclic 6-membered nitroxide moiety of formula (**A**) bonded to one or several **L**/**L'**:

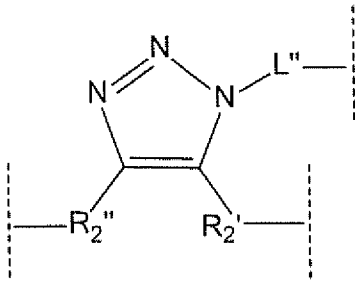


(**A**)

wherein R_1, R_2, R_3 and R_4, identical or different, are an alkyl (for instance, with 1 to 10 carbon atoms) or aryl group (for instance, with 6 to 12 carbon atoms), substituted or unsubstituted, or R_1 and R_2 and/or R_3 and R_4, as well as

R_1 and R_3 and/or R_2 and R_4 are linked together, thus, forming a cycloalkyl, for instance, with 5 to 12 carbon atoms, unsubstituted or substituted, for instance, with one or several phenyl. According to particular embodiments, R_1=R_2=R_3=R_4=methyl or R_1 and R_2, as well as R_3 and R_4, are linked together and form a cyclohexyl.

In particular, a moiety of formula (**A**) is bonded to one **L** or **L'** by the carbon atom which is in para to the NO$^{\bullet}$. For instance, L=L' and represent (from the Si atom to the molecule carrying the radical X or Y):



with L" = $C_{1\text{-}6}$ alkyl or phenyl covalently bonded to Si and R"$_2$ and/or R_2' is (are) covalently bonded to X or Y. For instance, if R"$_2$ and/or R_2' is (are) covalently bonded to X or Y, R"$_2$ and/or R_2' = CH_2-O. If R"$_2$ or R_2' is not covalently bonded to X or Y, the considered R"$_2$ or R_2' may be replaced by a hydrogen atom.

The materials used in the D-DNP according to the invention are, for instance, in the form of a powder and ideally, in the form of a bulk porous solid, which are compatible for their use as an electron source for DNP, and in particular, for D-DNP, where they will be impregnated with a liquid containing the analyte. A bulk porous material is a material which preferentially presents at least one dimension higher than 100 nm, preferentially higher than 10 µm. A dimension of a material corresponds to a distance between two points of a material and can be directly measured on the material or on a photography of the material, taken by electronic microscopy. In particular, according to the invention, the material used in the D-DNP has its larger dimension which is higher than 1 µm, preferentially higher than 10 µm.

The materials used in the D-DNP according to the present invention are porous and can be either structured or non-structured materials. It should be noted that the former layer obtained by sol-gel treatment in some embodiments can be structured while the starting porous solid is not structured and vice versa. The material is composed of pores and walls.

In some embodiments, in the material used in the D-DNP according to the invention, the porous network corresponding to the initial porous existing solid is structured in a hexagonal array of the pores or in a cubic or worm-like arrangement of the pores.

The structuration of a material or a layer corresponds to the long-range spatial ordering of the pores (cage like pores or pore-channels) into a network which can present several types of organization. The organization/structuration or the non-structuration of a material can be analyzed by Small-Angle X-ray diffraction (XRD) and electron microscopy. The Small-Angle XRD is performed on a powder sample using the CuKα radiation (λ = 0.154 nm). The diffraction patterns are usually collected in the 2Θ angle range [0.5° - 10.0°], for instance, at a scanning rate of 0.1 °/min.

A non-structured material can be defined as a material which presents no peak on its Small-Angle XRD diffractogram measured by a man skilled in the art. It should be noted that in some rare cases, a form on a Small-Angle XRD diffractogram can be observed which, if not related to an artefact of the analysis, should not have a Full Width Half Maximum (FWHM, expressed is 2θ) smaller or equal to 0.5°.

On the contrary, a structured material can be defined as a material, which presents at least one peak on its Small-Angle XRD diffractogram. The peak(s) which can be visualized on the diffractogram is (are) characteristic of the presence of the porous organization into the analysed samples. A structured layer may have weak diffraction peak, depending on its thickness.

When more than one diffraction peak is observed on the Small-Angle XRD diffractogram, the organization of the porous network can be accurately determined and the interplane spacings, d(hkl) for different Miller indices (hkl) can be calculated using the Bragg's law (nk = 2dsinΘ). So, it is possible to

determine if the network has a hexagonal or a cubic organization for instance. In the case of non-structured materials, no peaks are observed by Small-Angle XRD.

When an hexagonal arrangement of the pore network is present in the sample, a minimum of three diffraction peaks corresponding to the interplane spacings with following Miller indices (1,0,0), (1,1,0), (2,0,0) are observed on the Small-Angle XRD diffractogram.

For cubic arrangements, several spaces groups can be observed by Small-Angle XRD depending on the indexation of the diffraction peaks:

- with at least 3 peaks indexed as (1,1,0), (2,0,0) and (2,1,1) reflections, the cubic structure with *Im3m* space group is characterized,
- with at least 3 peaks indexed as (1,1,1), (2,2,0) and (3,1,1) reflections, the cubic structure with *Fm3m* space group is characterized,
- with at least 3 peaks indexed as (2,0,0), (2,1,0) and (2,1,1) reflections, the cubic structure with Pm3m space group is characterized.

The physical property and texture of the material can be studied by transmission electron microscopy. The hexagonal or cubic can also be easily confirmed by transmission electron microscopy. The obtained micrographs clearly show the long-range periodicity of the porous network. Non-structured materials or worm-like structures present characteristic and distinguishable micrographs of porous sponge-like grains.

The physical property and texture of the non-structured material can also be studied by transmission electron microscopy. The obtained micrographs clearly show the lack of organization in the material which is porous sponge-like.

In the case of very large pores (for instance >0.5 µm), water porosity can be performed to estimate the porosity, i.e. the pore volume, of a material by simple gravimetric method according to which the weight of water required to water-saturate a dry sample is divided by the weight of the dry material.

To determine more accurately the porosity and determine the texture and the porosity data of the non-structured materials, two cases exist:

- if the pores are in the 0.2 to 200 nm range, the materials can be analysed by nitrogen adsorption and desorption measurements which are achieved at 77 K using specific apparatus. The isotherms obtained can be used by the man skilled

in the art to distinguish the type of materials prepared, for example, to distinguish non-structured from structured materials having hexagonal, cubic or worm-like pores arrangement. The adsorption isotherm can be used to measure the total pore volume using data ranging from $0 < P/P_0 < 0.990$ (P/P_0 standing for the relative pressure in the cell), in the case that all the pores are smaller than 200 nm diameter. The specific surface area (S_{BET}) can be calculated by Brunauer–Emmett–Teller (BET) equation. The pore diameter distribution and the mean pore diameter can be calculated using Barrett–Joyner–Halenda (BJH) method from the adsorption branch of the N_2 adsorption-desorption isotherm.

- if the pores are in the 200 nm to 800 µm range, the materials can be analysed by Mercury Intrusion Porosimetry using specific apparatus. For an estimation of the corresponding mean pore diameter from the applied pressure (in bars) the Washburn equation with the surface tension of mercury of 480 dynes/cm and a contact angle of mercury on a silica surface of 140° can be used. It should be noted that mercury porosimetry can be used to analyse pores as low as 10 nm, even if in that case, this method is not preconized for measuring the porosity of the materials used in the invention.

In general, the total pore volume or porosity of a material will be accurately measured by a man skilled in the art, using a technique adapted to the material textural properties. The materials can have a single pore size distribution or several. For instance, a material having bis-distributed pore size is a single material having pores with a size centred at 20 nm and at 1 µm.

Preferably, the materials used in the D-DNP according to the invention have monodistributed pore size with a mean pore diameter from 2 nm to 20 µm, more preferably from 3.5 nm to 2 µm, and preferentially from 3.5 to 500 nm and more preferentially from 3.5 to 30 nm. Non-structured pore size distribution is broader (typically, more than ± 20 % and until ± 100%) than the one in structured materials that present a narrow pore distribution (typically ±20% or less).

Such porous materials, in particular, with mean pore diameter (d_p) from 2 nm to 20 µm, present large porous volume, typically from 0.3 to 230 $cm^3.g^{-1}$, and advantageously in the range of 3.5 to 500 nm and from 0.7 to 150 $cm^3.g^{-1}$ respectively. This is particularly interesting for DNP applications in particular,

because such porosity allows the introduction of a larger volume of liquid containing the analyte of interest by impregnation (when compared to non-porous materials). Moreover, the materials having large pores (mean pore diameter (d_p) more than 3.5 nm) are particularly interesting for the introduction of complex – larger – analyte systems. Materials which are either poorly porous or with small pores are therefore less interesting.

The range of radicals concentration defined as radical loading (µmol of radicals.g^{-1}) selected for the materials used in the D-DNP according to the invention, with the regular distribution of the radicals obtained by the sol-gel process or by the grafting one is particularly interesting for DNP application, because it minimizes the radical deactivation referred as quenching, observed when radicals are very close to each other (phenomenon more pronounced when radical loading higher, that is when the radical concentration is higher). The radical density can be determined by using electron magnetic resonance spectroscopy (EPR), which allows the measurement of the number of electrons (radicals) per gram. The loading is obtained by placing the dry sample in powder form in a glass tube, and recording the EPR spectrum at room temperature (for instance 25°C) at the X-band (9.52 GHz microwave frequency, conversion time = 40.96 ms, time constant = 5.12 ms, spectral widths = 600 Gauss, and 1024 data points, modulation frequency = 100 kHz, modulation amplitude = 1 Gauss, and microwave power set to avoid saturation of the signal), integrating the EPR signals, which are proportional to the number of spins (radicals) and by comparing them with the integrated spectrum of a standard solution of any persistent radical such as TEMPO. The radical density obtained is expressed in µmol_radical.g^{-1}.

In order to measure the peak-to-peak EPR linewidth (called hereinafter EPR linewidth) for the central signal of the CW spectra, the EPR experiments were performed under the conditions described above for electron magnetic resonance spectroscopy (EPR), but at 110 K and with an impregnation of the material with 1,1,2,2-tetrachloroethane. The EPR linewidth allows evaluating the inter-radical distances (r_e) distribution and therefore, the proximity of radicals also representative of the homogeneity of the sample. In fact, these inter-radical

distances can be determined by EPR *via* the inter-electron dipolar couplings, which rapidly decrease as a function of r_e^{-3}. The inter-electron dipolar coupling typically reduces when inter-radical distances are larger than 2 nm, beyond which the EPR linewidth stabilizes down to ca. 12 Gauss. In the material used in the D-DNP according to the invention, the EPR linewidth is preferably lower than 15 Gauss.

Description of the D-DNP application

The materials described in the invention are used as polarization agents, in the Dynamic Nuclear Polarization (DNP) technique, and more specifically, Dissolution DNP (D-DNP) that enacts the transfer of electron spin polarization towards the nuclei of an analyte. Any material described in the present invention, whatever the disclosed embodiment, can be used in the D-DNP techniques disclosed hereafter.

The aim of D-DNP, performed at temperature below 15 K, is to produce a liquid hyperpolarized analyte to be further used for Nuclear Magnetic Resonance (NMR) or Magnetic Resonance Imagery (MRI) analysis. The particular design of the materials described in the invention makes it possible to produce an optimal polarization transfer and an optimal increase in signals for the polarized nuclei of the analyte being studied, especially when Dissolution DNP is used. More specifically, the particular characteristics of the materials described in the invention make possible the polarization of any analyte dissolved in an aqueous solution without glassy agent such as glycerol or DMSO. The polarization transfer can be obtained at low temperatures (in particular < 15K, preferentially < 5 K) and high field (in particular > 2.5 T, preferentially B > 6 T).

The invention also concerns the use of a material described in the invention as an electron source for dissolution dynamic nuclear polarization.

The invention also concerns a process for polarizing ^{1}H, ^{13}C or another nucleus within an analyte by dissolution dynamic nuclear polarization (D-DNP), said process comprising the successive steps of:

i) providing a liquid sample containing the analyte;

ii) impregnating a material described in the invention with the liquid sample containing the analyte,

iii) cooling the impregnated material, at a temperature in the range from 0.5 K to 300 K, preferably in the range of 0.5 K to 15 K, and more preferably in the range of 0.5 K to 5 K ;

iv) submitting the impregnated material in the frozen state obtained in step iii), to DNP conditions to polarize the spins of the selected nucleus/nuclei of the analyte, in particular, including the application of a magnetic field and a microwave irradiation.

Optionally, this step iv) can include a cross polarization sequence during which the polarization of the nucleus polarized, in particular, the polarization of ^{1}H, is transferred to another nucleus of the analyte.

In the liquid sample containing the analyte, the analyte will preferably be in solution. So, a solvent or a mixture of solvents able to dissolve the analyte will preferentially be used. The process according to the invention can be used on any analyte of interest: organic ones (e.g. Na pyruvate) or inorganic ones (e.g. phosphate). For instance, the analyte of interest comprises any nucleus with spin ½ such as ^{1}H, ^{13}C, ^{31}P, ^{15}N, ^{29}Si, ^{89}Y and/or ^{19}F atoms and/or any nucleus with quadrupolar spin such as ^{27}Al atoms which are analyzed. For Magnetic Resonance Imagery (MRI) application, the analyte will be, for instance, a metabolite, i.e. a molecule that is involved in one of several human cell fast metabolisms.

The solvent used in the liquid sample for impregnation depends on the nature of the analyte and on the final application. For Magnetic Resonance Spectroscopic Imaging (MRSI) applications, whatever material is used, before the analysis, the dry material used for DNP will be impregnated with a liquid containing the analyte that will be polarized. This liquid sample should be compatible with human physiology, i.e. the analyte should be biocompatible, metabolisable molecules or non-metabolisable, as well as the solvent, typically water. Eventually, if the liquid containing the analyte is not compatible with human physiology, it should be treatable to be so within less than half of the relaxation time (T1) of the molecule in the conditions, the T1 considered here

being under conditions of the purification (field, temperature, solution composition...).

For NMR application after dissolution, whatever the material used is, before the analysis, the material used for DNP will be impregnated with a liquid sample of analyte that will be polarized. This liquid sample can be made in water, glycerol or in any other solvent or combination of solvents, chosen for instance among those listed by Zagdoun et al. Chem. Commun. 2012, 48, 654-656, particularly toluene, chloroaromatics, chloroalkanes and bromoalkanes.

Whatever the final application is, the liquid sample can also include organic molecules (small or large like proteins or polymers), salts or other compounds such as phosphate buffer. Before polarization, it is advantageous to obtain a mixture of the liquid sample and the materials as homogeneous as possible.

The impregnation step will be carried out by any convenient method, for example, using the Incipient Wetness Impregnation technique as illustrated in [http://pubs.acs.org/JACSbeta/scivee/index.html#video2] and as described in the following books: K.P. de Jong, *Synthesis of Solid Catalysts*, Wiley, **2009** and G. Ertl, et al., *Preparation of Solid Catalysts*, Wiley, **1999**. An incipient wetness impregnation (IWI) is made by impregnating the dry material with a volume of solution corresponding to the pore volume of the material ±50%. The concentration of the analyte in the liquid sample used for impregnation will, preferentially be chosen for obtaining a concentration of analyte per gram of material in the range of 9×10^{-4} to 5 $mol.g^{-1}$, preferentially, in the range 2×10^{-3} to 3.3 $mol.g^{-1}$.

For the polarization of an analyte adsorbed in the material described in the invention, the impregnated material with the liquid sample containing the analyte is cooled at a temperature in the range from 0.5 K to 300 K, preferably in the range of 0.5 K to 15 K, and more preferably in the range of 0.5 K to 5 K, before the submission to DNP conditions. In general, this cooling leads to the solidification of the liquid sample containing the analyte. This cooling is classically obtained with a Helium bath at atmospheric pressure down to 4.2 K or under reduced pressure to reach lower temperature.

The polarization of the analyte in step iv) is obtained by submitting the impregnated material with the liquid sample containing the analyte, to DNP conditions to polarize the selected nuclear spins present in the analyte: ^{1}H nuclear spin, ^{13}C nuclear spin, or another nuclear spin for instance chosen among ^{31}P, ^{15}N, ^{29}Si, ^{89}Y ^{19}F atoms and ^{27}Al, by application of a magnetic field and of a microwave irradiation. When the analyte comprises several atoms of the selected nuclear spin, all the spins of all those atoms will be polarized. The power and the frequency of the microwave irradiation will be selected by the man skilled in the art considering the nuclear spin to polarize and the conditions used, for instance, the magnetic field. The polarization transfer requires continuous microwave irradiation at a frequency close to the corresponding electron paramagnetic resonance (EPR) frequency, for instance $f_{\mu w}^{+}$ = 187.85 (positive polarization) or $f_{\mu w}^{-}$ = 188.3 GHz (negative polarization) at 6.7 T and 1.2K for TEMPO radical. Preferably, a frequency modulation of the applied microwave irradiation is used.

The analyte is polarized by microwave irradiations in a magnetic field in the range of 2 to 24 T, preferentially in the range of 3 to 15 T, and more preferentially, in the range of 6 to 12 T and/or at low temperature, in particular, in the range from 0.5 K to 300 K, preferably in the range of 0.5 K to 15 K, and more preferably, in the range of 0.5 K to 5 K. The radical linked to the material plays a central role for the generation of the nucleus polarization. Classically, the polarization is transferred from the unpaired electrons of the covalently linked radicals carried by the material described in the invention to nuclei of the analyte by the saturation of the electron transitions upon microwave irradiation. The polarization of step iv) may be performed in a polarizer equipped with a microwave source adapted to DNP (able to generate irradiation in the GHz range).

In step iv) described above, direct polarization of a selected nuclear spin (direct polarization) or CP-DNP (cross-polarization DNP) through proton can be performed. In CP-DNP, the polarization is first directly transferred from the electron to the ^{1}H nuclei of the impregnated material described in the invention, and is then transferred to another nucleus by Hartmann-Hahn $^{1}H \rightarrow {}^{A}X$ cross-polarization (Jannin S. et al. *Chem. Phys. Lett.* **2011**, 517, 234; Bornet A. et al.

Appl. Magn. Reson. **2012**, 43, 107; Jannin S. et al. *Chemical Physics Letters* **2012**, 549, 99; Bornet A. et al. *Journal of Physical Chemistry Letters* **2013**, 4, 111; Batel M. et al. *Chemical Physics Letters* **2012**, 554, 72, patent application WO2013153101A1), in particular to ^{13}C and ^{15}N.

Therefore, the invention also provides a process for polarizing the spins of a nucleus or nuclei within an analyte by dynamic nuclear polarization (DNP), said process comprising a step of polarizing a ^{1}H nuclear spin within an analyte by dynamic nuclear polarization (DNP) described above, and said process further comprising the step of cross-polarization (CP) from ^{1}H nuclei to other nuclei, preferentially ^{13}C or ^{15}N.

Advantageously, after step iv) of polarization, the impregnated material is warmed and a solution is passed through the material which will carry the polarized analyte with it. Preferably, the warming is carried out by passing the solution at a convenient temperature. Two steps: first warming of the material and secondly, passing the solution, are also possible.

A material described in the invention is particularly suitable to be used as a polarizing agent in DNP applied to dissolution DNP (D-DNP). A process for polarizing ^{1}H, ^{13}C or another nucleus within an analyte by dissolution dynamic nuclear polarization (DNP), comprises the steps i) to iv) previously disclosed, the polarizing steps being followed by the warming of the impregnated material and the circulation of a solution through the material. By passing within the material, this solution will carry with it the obtained polarized analyte and, as a result, a solution of the polarized analyte is obtained and is made available for direct analysis (NMR) or further use (injection into animal/patient followed by MRI). This step v) is commonly designed as "dissolution".

The passed solution consists, for instance, in a solvent or in mixture of solvents, chosen among water, deuterated water or a buffered aqueous solution. In particular, this solution before passing through the material is at a temperature in the range of 333 K to 473 K and, for instance, at a pressure ranging from 2 to 15 bars depending of the solvents. The amount and temperature of the solution is adjusted by the man skilled in the art, so that the solution obtained after the "dissolution step" including the polarized analyte has

the desired temperature, that is, in general, a temperature comprised between anatomic and room temperature (298-313 K).

The time between the obtaining of the polarized analyte solution after dissolution step v) and the end of the polarizing step iv) is generally in a range from 5 to 25 seconds. For more details, we can refer to US 20140091792 A1 ("Method for hyperpolarization transfer in the liquid state"). At that stage, the solution is readily available for any application (it can be transferred in a syringe for *in vivo* MRI/MRS study or into a NMR tube).

After, the NMR spectra/MRI images of the selected nucleus/nuclei (i) of the polarized analyte can be recorded in a NMR spectrometer/MRI spectrometer.

The invention also concerns a method of analysis by Nuclear Magnetic Resonance (NMR) or Magnetic Resonance Imagery (MRI) of one or more selected nuclei of an analyte of interest, wherein it uses dynamic nuclear polarization generated with a material described in the invention, and in particular, the NMR or MRI methods which implement, in a prior step, a process for polarizing by dissolution dynamic nuclear polarization according to the invention. According to one embodiment, such a method implements a polarizing step of a ^{1}H nuclear spin, a ^{13}C nuclear spin, or another nuclear spin of the analyte according to a process for polarizing ^{1}H nuclei, ^{13}C nuclei, or other nuclei of the analyte, as previously disclosed. According to these embodiments, such a method implements a direct polarizing step from the material electrons (radicals) to a ^{1}H nuclear spin, a ^{13}C nuclear spin, or of a nuclear spin other than ^{1}H or ^{13}C of the analyte, for instance, chosen among ^{31}P, ^{15}N, ^{29}Si, ^{89}Y, ^{19}F and ^{27}Al. The ^{1}H polarization can also be subsequently cross-polarized to another nucleus of interest as previously disclosed. So, the invention also concerns a method wherein a polarizing step for polarizing a nucleus is performed by polarization transfer (cross-polarization) from polarized ^{1}H.

The following examples, in reference to the annexed Figures, illustrate the invention.

Figure 1 is a schematic presentation of the materials HYPSO 5 (xx) 1/yy and HYPSO 6 (xx) 1/yy preparation routes involving two steps: first surface treatment, then the alkyne-azido coupling chemical step to attach the radical.

Figure 2 shows TEM pictures of hexagonally structured HYPSO 2 (53) 1/140 (left) and HYPSO 5 (26) 1/420 made using non-structured silica (right).

Figure 3 presents the variation of P(^{1}H) with the radical concentration of HYPSO 2, 5 and 6 at 4.2 K with modulation.

Figure 4 presents the variation of P(^{1}H) with the radical concentration of HYPSO 2, 5 and 6 at 1.2 K with modulation.

Figure 5 presents the DNP build-up curves with modulation together with the exponential fits for HYPSO 2 (94) 1/100, HYPSO 5 (26) 1/420, HYPSO 5 (53) 1/284 and HYPSO 6 (45) 1/320.

Figure 6 presents the ^{1}H->^{13}C CP-DNP build-up curves for HYPSO 2 (94) 1/100, HYPSO 5 (53) 1/284 and HYPSO 6 (45) 1/320.

PREPARATION AND CHARACTERIZATION OF MATERIALS

1. Nomenclature:

- ***HYPSO 2 (xx) 1/yy***: Hexagonal structured SiO_2-based material (SBA-15), TEMPO radical incorporation via Copper-Catalysed Azide-alkyne cycloaddition (Cu-AAC) – comparative example : the azidopropyl is directly introduced during the synthesis of the SBA-15.

- ***HYPSO 5 (xx) 1/yy***: Non-structured SiO_2-based material prepared using a commercial silica SiO_{2_A} (Sylopol 948 von Grace Davison from LyonDellBasell) and grafting of $(OEt)_3SiC_3H_6N_3$, TEMPO radical incorporation via Copper-Catalysed Azide-alkyne cycloaddition (Cu-AAC).

- ***HYPSO 6 (xx) 1/yy***: Non-structured SiO_2-based material prepared using a commercial silica SiO_{2_A} (Sylopol 948 von Grace Davison from LyonDellBasell) and surface co-gel, TEMPO radical incorporation via Copper-Catalysed Azide-alkyne cycloaddition (Cu-AAC)

- ***HYPSO 10 (xx) 1/yy***: Non-structured SiO_2-based material prepared using a commercial silica SiO_{2_B} (Silica SiliaSpheres from Silicycle) and surface co-

gel, TEMPO radical incorporation via Copper-Catalysed Azide-alkyne cycloaddition (Cu-AAC).

- ***HYPSO 11 (xx) 1/yy***: 2D-Hexagonal structured SiO_2-based material (SBA-15), and surface co-gel, TEMPO radical incorporation via Copper-Catalysed Azide-alkyne cycloaddition (Cu-AAC),

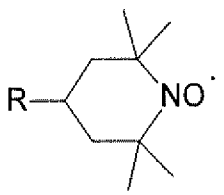
- ***HYPSO 12 (xx) 1/yy***: 2D-Hexagonal structured SiO_2-based material (SBA-15), and surface co-gel, TEMPO radical incorporation via Copper-Catalysed Azide-alkyne cycloaddition (Cu-AAC), after two surface funtionalizations.

which for "xx" stands the surface density of radical in the material ($\mu mol_{R\bullet}.g^{-1}$), determined by EPR. "1/yy" stands for the initial molar ratio 3-azidopropyltrimethoxysilane to TEOS.

The material are referred as 1/yy-R-Mat where "1/yy" stands for the initial 3-azidopropyltrimethoxysilane to TEOS molar ratio, "R" stands for the nature of the organic function ($-N_3$ or TEMPO) and "Mat" stands for the type of material ($SiO_{2_A_sc}$, $SiO_{2_A_scg}$, $SiO_{2_B_scg}$ or SBA-15 or $SBA\text{-}15_{_scg}$). $SiO_{2\ A_sc}$ and $SiO_{2_A_scg}$ stand here for commercial amorphous silica Sylopol 948 von Grace Davison from purchase from LyonDellBasell after surface treatment, respectively surface condensation and surface cogel. $SiO_{2_B_scg}$ stands here for commercial amorphous silica from Silicycle after surface treatment, by surface cogel. SiO_{2_A} stands for Silica Grace from LyonDellBasell (257 m^2/g, dp = 28 nm). SiO_{2_B} stands for Silica SiliaSpheres from Silicycle (452 m^2/g, dp = 6 nm). $SBA\text{-}15_{_scg}$ stands here for prepared structured $SBA\text{-}15_{_A}$ after surface treatment, by surface cogel. $SBA\text{-}15_{_A}$ stands for pure silica SBA-15 (893 m^2/g, dp = 9 nm).

TEMPO: 2,2,6,6-tetramethylpiperidin-1-oxyl

The compounds of formula :



are named R-TEMPO.

O-propargyl-TEMPO: 4-(propargyloxy)-2,2,6,6-tetramethylpiperidin-1-

oxyl

TEOS: Tetraethyl orthosilicate

THF: Tetrahydrofuran

DMF: Dimethylformamide

Et:ethyl

RT: room temperature

P123: Pluronic® 123 sold by BASF

2. Characterization of materials and instrumentation

2.1 Transmission electronic microscopy.

Conventional TEM micrographs were performed at the "Centre Technologique des Microstructures", UCBL, Villeurbanne, France, using a 2100F JEOL electron microscope operated at 200 kV. The samples were prepared by dispersing a drop of the ethanol suspension of a ground sample on a Cu grid covered by a carbon film.

2.2 X-Ray Diffraction.

Small-Angle X-ray diffraction (XRD) on powder was carried out with a Bruker D8 Avance diffractometer (33 kV & 45 mA) with CuKα radiation (λ = 0.154 nm) in the Service Diffraction RX, IRCE Lyon, France. The diffraction patterns were collected in the 2θ angle range [0.45°-7.0°] at a scanning rate of 0.1°/min. The interplane spacings, d(hkl) for different Miller indices (hkl) were calculated using the Bragg's law (nk = 2dsinθ). The lattice parameter (a0) for the hexagonal structured mesoporous material is given by a0 = 2d(100)/$\sqrt{3}$.

2.3 Nitrogen adsorption-desorption measurements.

The Nitrogen adsorption and desorption measurements were achieved at 77 K using a BELSORB-Mini from BEL-JAPAN. Before N_2 adsorption, the samples were outgassed at 10^{-4} Pa at 408 K for 12 h. The pore diameter distribution and the mean pore diameter (d_p) were calculated using Barrett–Joyner–Halenda (BJH) method. The specific surface area (S_{BET}) was calculated by Brunauer–

Emmett–Teller (BET) equation. The pore volume was measured from the adsorption isotherm using data ranging from $0 < P/P_0 < 0.990$ with P and P_0 the equilibrium and the saturation pressure of N_2 respectively. It should be noted that the pore volume measured by N_2 adsorption corresponds to the volume of pores smaller than 200 nm. The pores of the materials characterized in the examples are at least for 95% smaller than 200 nm in diameter; hence, the pore volume measured by N_2 adsorption is representative of the porosity of the material (other techniques such as mercury porosimetry was not required).

2.4 Electron Paramagnetic Resonance (EPR).

All Continuous Wave (CW) EPR spectra were recorded on an X-band Bruker EMX EPR spectrometer. Data analysis was performed using MatLab 2011 and Origin 8.5.

EPR spectra were recorded at X Band (9.52 GHz microwave frequency) with the following parameters: conversion time = 40.96 ms, time constant = 5.12 ms, modulation frequency = 100 kHz, modulation amplitude = 1 Gauss, spectral width = 600 Gauss, and 1024 data points, microwave power adjusted to avoid saturation of the signal.

2.5 EPR Peak-to-peak linewidth.

The samples for line shape analysis were prepared as follows: dry TEMPO Material was wet by incipient wetness impregnation with 1,1,2,2-tetrachloroethane in air. The samples were filled in a 3.2 mm EPR quartz tube. The sample height in the tube was for all materials between 3 and 5 mm. EPR spectra were recorded at 110 K using a nitrogen flow cryostat. Attenuation was varied from 32 to 23 dB. The EPR spectrum of a nitroxide radical consists of three lines due to strong hyperfine interaction with the ^{14}N nucleus. For the EPR linewidth measurements, we have used the central line, which is least broadened by the g-tensor and hyperfine anisotropies and which therefore is the most sensitive to the dipolar broadening. The EPR linewidth was determined using the difference between the minimum and the maximum of the central line, also called peak-to-peak linewidth (Gerson, F.; Huber, W. In *Electron Spin Resonance*

Spectroscopy of Organic Radicals; Wiley-VCH Verlag GmbH & Co. KGaA: 2004). For the obtained signal to noise levels, the estimated linewidth error bars were in the order of 5 %.

2.6 EPR spin count

Samples for spin count experiments were prepared as follows: the dry powder was filled in a glass capillary (50µL Hirschmann ring caps), and the bottom was closed with putty. The sample height was around 19 mm, and the weights were recorded for all samples. CW EPR spectra were recorded at room temperature. The quantification of the EPR signal was performed by using the double integral of the CW spectra corrected for microwave power, receiver gain and sample weight. Determination of the quantity of radical per gram was obtained by comparison to a standard TEMPO solution (4.07 mM in Toluene), and expressed in radical per surface area as evaluated from N_2 adsorption measurement.

3. Comparative EXAMPLE – 1/yy-TEMPO-SBA-15 (HYPSO 2) with three different concentration – Hexagonal SBA-15 materials with TEMPO radical moiety introduced through alkyne-azide cycloaddition

These materials were prepared according to Gajan, D., et al. (2014). "Hybrid polarizing solids for pure hyperpolarized liquids through dissolution dynamic nuclear polarization." Proceedings of the National Academy of Sciences of the United States of America 111(41): 14693-7.

3.1 Preparation of 1/140-N3-SBA-15 materials - Representative procedure

Preparation of 1/140-N3-SBA-15 material

P123 (7.1 g) dissolved in an aqueous HCl solution (290 mL, pH = 1.5) was added in a mixture of TEOS (16.8 mL, 80.8 mmol) and 3-azidopropyltrimethoxysilane (143 mg, 0.58 mmol) at 25 °C (composition of the mixture: 140 TEOS to one 3-azidopropyltriethoxysilane). The reaction mixture was stirred for 3 h giving rise to a microemulsion (transparent mixture). To the solution heated to 45 °C, sodium fluoride (120 mg, 2.9 mmol) was added under stirring. The mixture was stirred at 45°C for 72 hours. The resulting solid was

filtered and washed with water (3 × 100 mL) and acetone (3 × 100 mL). The surfactant was removed with ethanol using a soxhlet extractor for 48h. After filtration, washing with ethanol and ether, and drying at 135 °C under vacuum (10–5 mbar) for 12 h led to **1/140-N3-SBA-15** (ca. 5 g) as a white solid.

Preparation of 1/100-N3-SBA-15 material

1/100-N3-SBA-15 material was prepared following the above-described procedure (cf. **1/140-N3-SBA-15 material**) using 4.82 g of P123; aqueous HCl solution (200 mL, pH = 1.5); TEOS (11.55 g, 55.44 mmol); 3-azidopropyltrimethoxysilane (137 mg, 0.554 mmol); NaF (82 mg, 1.96 mmol); **1/100-N3-SBA-15 material** (3.4 g).

Preparation of 1/60-N3-SBA-15 material

1/60-N3-SBA-15 material was prepared following the above-described procedure (cf. **1/140-N3-SBA-15 material**) using 4.89 g of P123; aqueous HCl solution (200 mL, pH = 1.5); TEOS (11.47 g, 55.1 mmol); 3-azidopropyltrimethoxysilane (228.3 mg, 0.92 mmol); NaF (82.6 mg, 1.97 mmol); **1/60-N3-SBA-15 material** (3.4 g).

3.2 Preparation of 1/140-TEMPO-SBA-15 or HYPSO 2 (53) 1/140 through Cu(I)-catalyzed azide-alkyne cycloaddition (Cu-AAC) - Representative procedure

O-propargyl TEMPO [A. Gheorghe, A. Matsuno, O. Reiser, Adv. Synth. Cat. 2006, 1016-1020]

Under an argon atmosphere was NaH (2.72 g, 67.9 mmol) added to dry DMF (300 mL) and cooled to 0 °C. To this suspension TEMPOL (9.00 g, 52.2 mmol) was added in portions. The reaction mixture was stirred 30 min at 25 °C and then cooled again to 0 °C before propargyl bromide (80 wt% in toluene, 10.1 g, 67.9 mmol) was added dropwise. The resulting reaction mixture was then stirred for 3 h at 25 °C. Then, H_2O (300 mL) was added and the product was extracted with EtOAc (3 × 150 mL). The combined organic layers were dried with

brine and Na_2SO_4 and fully concentrated under reduced pressure. Column chromatography (heptane → 10% EtOAc in heptane) yielded O-propargyl TEMPO (6.93 g, 63%) as an orange solid.

Preparation of HYPSO 2 (53) 1/140

Under an argon atmosphere, O-propargyl TEMPO (248 mg, 1.18 mmol) was added to a suspension of **1/140-N3-SBA-15 material** (2 g, 0.236 mmol azide) in DMF (24 mL) and Et_3N (1.1 mL). Then a solution of CuI (2.2 mg, 12 µmol) in DMF/Et_3N (1:1, 180 µL) was added. The mixture was stirred for 72 h at 50 °C and then filtrated and washed with DMF (2 × 20 mL), EtOH (3 × 20 mL), Et_2O (2 × 20 mL). The product was then dried under vacuum (10-5 mbar) at 100 °C for 15h.

Preparation of HYPSO 2 (94) 1/100

Under an argon atmosphere, O-propargyl TEMPO (342 mg, 1.63 mmol) was added to a suspension of **1/100-N3-SBA-15 material** (2 g, 0.325 mmol azide) in DMF (20 mL) and Et_3N (880 µL). Then a solution of CuI (3.1 mg, 16 µmol) in DMF/Et_3N (1:1, 240 µL) was added. The mixture was stirred for 72 h at 50 °C and then filtrated and washed with DMF (2 × 20 mL), EtOH (3 × 20 mL), Et_2O (2 × 20 mL). The product was then dried under vacuum (10-5 mbar) at 100 °C for 15h.

Preparation of HYPSO 2 (115) 1/60

Under an argon atmosphere, O-propargyl TEMPO (241.9 mg, 1.15 mmol) was added to a suspension of **1/100-N3-SBA-15 material** (2 g, 0.23 mmol azide) in DMF (23 mL) and Et3N (1.07 mL). Then a solution of CuI (2.2 mg, 12 µmol) in DMF/Et3N (1:1, 173 µL) was added. The mixture was stirred for 72 h at 50 °C and then filtrated and washed with DMF (2 × 20 mL), EtOH (3 × 20 mL), Et2O (2 × 20 mL). The product was then dried under vacuum (10-5 mbar) at 100 °C for 15h.

4. EXAMPLE 1 - 1/yy TEMPO $SiO_{2_A_sc}$ (HYPSO 5) with four different concentrations – Grafting of $(OEt)_3SiC_3H_6N_3$ at the surface of commercial non-structured silica followed by TEMPO radical incorporation via Copper-Catalysed Azide-Alkyne cycloaddition (Cu-AAC).

4.1 Preparation of 1/yy _N_3_$SiO_{2_A_sc}$ material. Representative procedure.

Figure 1 is a schematic presentation of the materials HYPSO 5 (xx) 1/yy and HYPSO 6 (xx) 1/yy preparation routes involving two steps: first surface treatment, then the alkyne-azido coupling chemical step to attach the radical.

Preparation of 1/284 N_3 $SiO_{2_A_sc}$ material. General procedure

Silica SiO_{2_A} is dried at 150°C under vacuum (10–5 mbar) for 12 h. Under an argon atmosphere, the dry solid (5g) is then dispersed in 25 mL of dry toluene. At RT, Triethoxy Azidopropyl silane (72 mg, 293 mmole) dissolved in 25 mL of dry toluene is added to the solid in suspension (total toluene: 10mL/gSiO_2). The mixture is stirred for 1h at room temperature and heated to reflux for 24h minimum. The resulting solid is then filtered, and washed with toluene (3 × 100 mL), isopropanol (3 × 100 mL), diethyl ether (3 × 100 mL), and dried at 135 °C under vacuum (10–5 mbar) for 12 h led to **1/284_N_3_$SiO_{2_A_sc}$** (ca. 10 g) as a white solid.

Preparation of 1/104 N_3 $SiO_{2_A_sc}$ material.

1/104_N_3_$SiO_{2_A_sc}$ material was prepared following the above-described procedure (cf. **1/284_N_3_$SiO_{2_A_sc}$ material**) using 1g of dry silica; dry toluene (12.9 mL); Triethoxy Azidopropyl silane (39.1 mg, 161 mmole) in 2.1 mL of dry toluene (73,7 mmol/L solution used); washing volumes: 30 mL; **1/104_N_3_$SiO_{2\text{-}A\ sc}$ material** (0.95g).

Preparation of 1/157 N_3 $SiO_{2_A_sc}$ material.

1/157_N_3_$SiO_{2_A_sc}$ material was prepared following the above-described procedure (cf. **1/284_N_3_$SiO_{2_A_sc}$ material**) using 1g of dry silica; dry toluene (13.6 mL); Triethoxy Azidopropyl silane (26.0 mg, 105 mmole) in 1.4 mL of dry toluene (73,7 mmol/L solution used); washing volumes: 30 mL;

1/157_N_3_$SiO_{2\text{-}A_sc}$ material (0.95g).

Preparation of 1/420 N_3 $SiO_{2_A_sc}$ material.

1/420_N_3_$SiO_{2_A_sc}$ material was prepared following the above-described procedure (cf. **1/284_N_3_$SiO_{2_A_sc}$ material**) using 1g of dry silica; dry toluene (14.5 mL); Triethoxy Azidopropyl silane (9.9 mg, 105 mmole) in 0.5 mL of dry toluene (73,7 mmol/L solution used); washing volumes: 30 mL; **1/420_N_3_$SiO_{2_A_sc}$ material** (0.95g).

4.2 Preparation of 1/yy_TEMPO_$SiO_{2_A_sc}$ (HYPSO 5) through Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC) - Representative procedure

Preparation of 1/284 TEMPO $SiO_{2_A_sc}$ material - HYPSO 5 (53). General procedure

Under an argon atmosphere, O-propargyl TEMPO (73.6 mg, 0.35 mmol) was added to a suspension of **1/284_N_3_$SiO_{2_A_sc}$** (2 g, 0.117 mmol azide) in DMF (11.7 mL) and Et_3N (410 µL). Then, a solution of CuI (4.4 mg, 23 µmol) in DMF/Et_3N (1:1, 350 µL) was added. The mixture was stirred for 60 h at 50 °C and then filtrated and washed with DMF (3 × 20 mL), EtOH (3 × 20 mL), Et_2O (3 × 20 mL). The product was then dried under vacuum (10-5 mbar) at 100 °C for 15h.

Preparation of 1/104 N_3 $SiO_{2_A_sc}$ material - HYPSO 5 (122).

Under an argon atmosphere, O-propargyl TEMPO (83 mg, 0.395 mmol) was added to a suspension of **1/104_N_3_$SiO_{2_A_sc}$** (0.5 g, 0.079 mmol azide) in DMF (7.9 mL) and Et_3N (370 µL). Then a solution of CuI (0.8 mg, 3.9 µmol) in DMF/Et_3N (1:1, 120 µL) was added. The mixture was stirred for 60 h at 50 °C and then filtrated and washed with DMF (3 × 20 mL), EtOH (3 × 20 mL), Et_2O (3 × 20 mL). The product was then dried under vacuum (10-5 mbar) at 100 °C for 15h.

Preparation of 1/157 N_3 $SiO_{2_A_sc}$ material - HYPSO 5 (80).

Under an argon atmosphere, O-propargyl TEMPO (55 mg, 0.26 mmol) was added to a suspension of **1/157_N_3_$SiO_{2_A_sc}$** (0.5 g, 0.053 mmol azide) in

DMF (5.26 mL) and Et_3N (240 µL). Then, a solution of CuI (0.5 mg, 3 µmol) in DMF/Et_3N (1:1, 390 µL) was added. The mixture was stirred for 60 h at 50 °C and then filtrated and washed with DMF (3 × 20 mL), EtOH (3 × 20 mL), Et_2O (3 × 20 mL). The product was then dried under vacuum (10-5 mbar) at 100 °C for 15h.

Preparation of 1/420 N_3 $SiO_{2_A_sc}$ material - HYPSO 5 (26).

Under an argon atmosphere, O-propargyl TEMPO (10.4 mg, 0.050 mmol) was added to a suspension of **1/420_N_3_$SiO_{2_A_sc}$** (0.25 g, 0.010 mmol azide) in DMF (3 mL) and Et_3N (50 µL). Then a solution of CuI (0.09 mg, 5 µmol) in DMF/Et_3N (1:1, 70 µL) was added. The mixture was stirred for 48 h at 50 °C and then filtrated and washed with DMF (3 × 20 mL), EtOH (3 × 20 mL), Et_2O (3 × 20 mL). The product was then dried under vacuum (10-5 mbar) at 100 °C for 15h.

5. EXAMPLE 2 - 1/yy TEMPO $SiO_{2\ A\ scg}$ (HYPSO 6) with three different concentrations – Co-gel using $(OEt)_3SiC_3H_6N_3$ and TEOS at the surface of commercial non-structured silica followed by TEMPO radical incorporation via Copper-Catalysed Azide-Alkyne cycloaddition (Cu-AAC).

5.1 Preparation of 1/yy_N_3_$SiO_{2_A_scg}$ material. Representative procedure.

Figure 1 is a schematic presentation of the materials HYPSO 5 (xx) 1/yy and HYPSO 6, 10, 11 & 12 (xx) 1/yy preparation routes involving two steps: first surface treatment, then the alkyne-azido coupling chemical step to attach the radical.

Preparation of 1/320 N_3 $SiO_{2\ A\ scg}$ material. General procedure

Silica SiO_{2_A} is dried at 150°C under vacuum (10–5 mbar) for 12 h. The dry solid (1 g, weighted under argon atmosphere) is dispersed in 20 mL of pure dioxane, then 1.4 mL of 2.3 mol.L^{-1} HCl solution is added. The solution is then heated in a closed vessel to 70°C. A solution (9 mL) containing Triethoxy Azidopropyl silane (12.9 mg, 52 µmol), TEOS (122.5 mg, 588 µmol), and 8.9 mL

of clean dioxane is added dropwise over a period of 15-20min under stirring. The mixture is then refluxed for about 1 h. The product is then filtered and washed consecutively with 20/80 water/EtOH (3 × 50 mL), EtOH (3 × 50 mL), and Et_2O (3 × 50 mL), and dried at 135 °C under vacuum (10–5 mbar) for 12 h led to **1/320_N_3_$SiO_{2_A_scg}$** (ca. 1 g) as a white solid.

Preparation of 1/150 N_3 $SiO_{2\ A\ scg}$ material.

The material was prepared following the above-described procedure (cf. **1/320_N_3_$SiO_{2_A_scg}$ material**) using dioxane (20 mL); 2.3M HCl solution (1.4 mL); 9 mL solution containing 3-azidopropyltrimethoxysilane (27.2 mg, 110 µmol), TEOS (110.4 mg, 530 µmol), dioxane (8.9 mL); washing volumes: 50 mL; **1/150_N_3_$SiO_{2_A_scg}$ material** (1g).

Preparation of 1/80 N_3 $SiO_{2\ A\ scg}$ material.

The material was prepared following the above-described procedure (cf. **1/320_N_3_$SiO_{2_A_scg}$ material**) using dioxane (10 mL); 2.3M HCl solution (0.7 mL); 4.5 mL solution containing 3-azidopropyltrimethoxysilane (25.4 mg, 102.5 µmol), TEOS (45.3 mg, 218 µmol), dioxane (4.4 mL); washing volumes: 25 mL; **1/80_N_3_$SiO_{2_A_scg}$ material** (1g).

5.2 Preparation of 1/xx_TEMPO_$SiO_{2_A_scg}$ (HYPSO 6) through Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC) - Representative procedure

Preparation of 1/320 N_3 $SiO_{2\ A\ scg}$ material – HYPSO 6 (45). General procedure

Under an argon atmosphere, O-propargyl TEMPO (16.4 mg, 0.078 mmol) was added to a suspension of **1/320_N_3_$SiO_{2_A_scg}$** (0.5 g, 0.026 mmol azide) in DMF (2.6 mL) and Et_3N (90 µL). Then, a solution of CuI (1.0 mg, 5.2 µmol) in DMF/Et_3N (1:1, 80 µL) was added. The mixture was stirred for 60 h at 50 °C and then filtrated and washed with DMF (3 × 20 mL), EtOH (3 × 20 mL), Et_2O (3 × 20 mL). The product was then dried under vacuum (10-5 mbar) at 100 °C for 15h.

Preparation of 1/150 N_3 $SiO_{2\ A\ scg}$ material – HYPSO 6 (95).

Under an argon atmosphere, O-propargyl TEMPO (34.7 mg, 0.165 mmol) was added to a suspension of **1/150_N_3_$SiO_{2_A_scg}$** (0.5 g, 0.055 mmol azide) in DMF (5.5 mL) and Et_3N (190 µL). Then a solution of CuI (2.1 mg, 11 µmol) in DMF/Et_3N (1:1, 170 µL) was added. The mixture was stirred for 60 h at 50 °C and then filtrated and washed with DMF (3 × 20 mL), EtOH (3 × 20 mL), Et_2O (3 × 20 mL). The product was then dried under vacuum (10-5 mbar) at 100 °C for 15h.

Preparation of 1/80 N_3 $SiO_{2\ A\ scg}$ material – HYPSO 6 (178).

Under an argon atmosphere, O-propargyl TEMPO (38.8 mg, 0.185 mmol) was added to a suspension of **1/80_N_3_$SiO_{2_A_scg}$** (0.3 g, 0.062 mmol azide) in DMF (6.15 mL) and Et_3N (0.22 mL). Then, a solution of CuI (2.3 mg, 12 µmol) in DMF/Et_3N (1:1, 0.18 mL) was added. The mixture was stirred for 60 h at 50 °C and then filtrated and washed with DMF (3 × 20 mL), EtOH (3 × 20 mL), Et_2O (3 × 20 mL). The product was then dried under vacuum (10-5 mbar) at 100 °C for 15h.

6. EXAMPLE 3 - 1/yy TEMPO $SiO_{2\ B\ scg}$ (HYPSO 10) with three different concentrations – Co-gel using $(OEt)_3SiC_3H_6N_3$ and TEOS at the surface of commercial non-structured silica followed by TEMPO radical incorporation via Copper-Catalysed Azide-Alkyne cycloaddition (Cu-AAC).

6.1 Preparation of 1/yy_N_3_$SiO_{2_B_scg}$ material. Representative procedure.

Figure 1 is a schematic presentation of the materials HYPSO 5 (xx) 1/yy and HYPSO 6, 10, 11 & 12 (xx) 1/yy preparation routes involving two steps: first surface treatment, then the alkyne-azido coupling chemical step to attach the radical.

Preparation of $SiO_{2\ B\ scg}$. General procedure

About 10 g of silica SiO_{2_B} is washed with 3 times 50 mL with ca. 10 g/L EDTA solution, then washed with ethanol 3 times 50 mL, then with diethyl ether 3 times 50 mL before to be dried at 150 °C under vacuum (10^{-5} mbar) for 12 h.

Preparation of 1/ 251 N_3 $SiO_{2_B_scg}$ material. General procedure

The dry solid 0.5 g, weighted under argon atmosphere) is dispersed in 10 mL of pure THF, then 0.7 mL of 2.3 mol.L^{-1} HCl solution is added. The solution is then heated in a closed vessel to 70°C. A solution (4.5 mL) containing Triethoxy Azidopropyl silane (8.4 mg, 33.9 µmol), TEOS (110.2 mg, 529 µmol), and 4.4 mL of clean THF is added dropwise over a period of 15-20 min under stirring. The mixture is then refluxed for about 1 h. The product is then filtered and washed consecutively with 20/80 water/ THF (3 × 50 mL), EtOH (3 × 50 mL), and Et_2O (3 × 50 mL), and dried at 135 °C under vacuum (10–5 mbar) for 12 h yielding **1/ 251_N_3_$SiO_{2_B_scg}$** (ca. 0.5 g) as a white solid.

Preparation of 1/ 420 N_3 SiO_{2_scg} material.

The material was prepared following the above-described procedure (cf. **1/ 251_N_3_$SiO_{2_B_scg}$ material**) using THF (10 mL); 2.3M HCl solution (0.7 mL); 4.5 mL solution containing 3-azidopropyltrimethoxysilane (5 mg, 20.34 µmol), TEOS (113 mg, 543 µmol), THF (4.4 mL); washing volumes: 50 mL; **1/ 420_N_3_$SiO_{2_B_scg}$ material** (0.5g).

Preparation of 1/ 606 N_3 $SiO_{2_B_scg}$ material.

The material was prepared following the above-described procedure (cf. **1/ 251_N_3_$SiO_{2_B_scg}$ material**) using THF (10 mL); 2.3M HCl solution (0.7 mL); 4.5 mL solution containing 3-azidopropyltrimethoxysilane (3.6 mg, 102.5 14.4 µmol), TEOS (45.3 114.3 mg, 549 µmol), THF (4.4 mL); washing volumes: 25 mL; **1/ 606_N_3_$SiO_{2_B_scg}$ material** (0.5g).

6.2 Preparation of 1/yy_TEMPO_$SiO_{2_B_scg}$ (HYPSO 10) through Cu(I)-catalyzed azide-alkyne cycloaddition (Cu-AAC) - Representative procedure

Preparation of 1/ 251 N_3 $SiO_{2_B_scg}$ material – HYPSO 10 (45). General procedure

Under an argon atmosphere, O-propargyl TEMPO (21.4 mg, 0.102 mmol) was added to a suspension of **1/ 251_N_3_$SiO_{2_B_scg}$** (0.5 g, 0.034 mmol azide) in DMF (3.4 mL) and . Then, a solution of CuI (1.28 mg, 6.7 µmol) in DMF/Et_3N

(5:2, 0.61 mL) was added. The mixture was stirred for 60 h at 50 °C and then filtrated and washed with DMF (3 × 20 mL), EtOH (3 × 20 mL), Et_2O (3 × 20 mL). The product was then dried under vacuum (10-5 mbar) at 55 °C for 12h.

Preparation of 1/ 420 N_3 SiO_2 $_{B\ scg}$ material – HYPSO 10 (95).

Under an argon atmosphere, O-propargyl TEMPO (12.8 mg, 0.061 mmol) was added to a suspension of **1/ 420_N_3_SiO_2_B_scg** (0.5 g, 0.020 mmol azide) in DMF 2 mL) and Et_3N (190 µL). Then a solution of CuI (0.78 mg, 4.09 µmol) in DMF/Et_3N 5:2, 0.37 mL) was added. The mixture was stirred for 60 h at 50 °C and then filtrated and washed with DMF (3 × 20 mL), EtOH (3 × 20 mL), Et_2O (3 × 20 mL). The product was then dried under vacuum (10-5 mbar) at 55 °C for 12h.

Preparation of 1/ 606 N_3 SiO_2 $_{B\ scg}$ material – HYPSO 10 (178).

Under an argon atmosphere, O-propargyl TEMPO (9.1 mg, 0.043 mmol) was added to a suspension of **1/ 606_N_3_SiO_2_B_scg** (0.5 g, 0.0144 mmol azide) in DMF (2 mL) . Then, a solution of CuI (0.50 mg, 2.63 µmol) in DMF/Et_3N (5:2 , 0.26 mL) was added. The mixture was stirred for 60 h at 50 °C and then filtrated and washed with DMF (3 × 20 mL), EtOH (3 × 20 mL), Et_2O (3 × 20 mL). The product was then dried under vacuum (10-5 mbar) at 55 °C for 12h

7. EXAMPLE 4 - 1/120 TEMPO SBA-15 $_{scg}$ (HYPSO 11) – Co-gel using $(OEt)_3SiC_3H_6N_3$ and TEOS at the surface of SBA-15 type structured silica followed by TEMPO radical incorporation via Copper-Catalysed Azide-Alkyne cycloaddition (Cu-AAC).

7.1 Preparation of SBA-15 $_A$ material. Representative procedure.

P123 (9.5 g) dissolved in an aqueous HCl solution (400 mL, pH = 1.5) was added in tetraethoxysilane (TEOS, 21.2 mL, 97 mmol) at 25 °C. The reaction mixture was stirred for 3 h giving rise to a micro-emulsion (transparent mixture). To the reaction mixture heated at 45 °C, a small amount of NaF (180 mg, 4.3 mmol)

was added under stirring. The mixture was left at 45°C under stirring for 72 h. The resulting solid was filtered, and washed three times with 100 mL of water and three times with 100 mL of acetone. The surfactant was removed by thermal treatment under a flow of dry air (100mL/min) at 500°C for 12h with a heating ramp of 1°C/min. The material was then evacuated under vacuum (10^{-5} mbar) for 2 h affording **SBA-15**$_{_A}$ (7.3 g) as a white solid.

7.2 Preparation of 1/120_N_3_SBA-15$_{_scg}$ material. Representative procedure.

Figure 1 is a schematic presentation of the materials HYPSO 5 (xx) 1/yy and HYPSO 6, 10, 11 & 12 (xx) 1/yy preparation routes involving two steps: first surface treatment, then the alkyne-azido coupling chemical step to attach the radical.

The dry solid of SBA-15$_{_A}$ (0.5 g, weighted under argon atmosphere) is dispersed in 10 mL of pure dioxane, then 0.7 mL of 2.3 mol.L^{-1} HCl solution is added. The solution is then heated in a closed vessel to 70°C. A solution (4.5 mL) containing Triethoxy Azidopropyl silane (16.9 mg, 68 µmol), TEOS (217 mg, 1044 µmol), and 4.2 mL of clean dioxane is added dropwise over a period of 15-20min under stirring. The mixture is then refluxed for about 1 h. The product is then filtered and washed consecutively with 20/80 water/EtOH (3 × 30 mL), EtOH (3 × 30 mL), and Et_2O (3 × 30 mL), and dried at 135 °C under vacuum (10–5 mbar) for 12 h affording **1/120_N_3_SBA-15**$_{scg}$ (ca. 0.5 g) as a white solid.

7.3 Preparation of 1/120_TEMPO_SBA-15$_{scg}$ (HYPSO 11) through Cu(I)-catalyzed azide-alkyne cycloaddition (Cu-AAC) - Representative procedure

Under an argon atmosphere, O-propargyl TEMPO (25.9 mg, 0.041 mmol) was added to a suspension of **1/120_N_3_SBA-15**$_{scg}$ (0.3 g, 0.041 mmol azide) in DMF (4.1 mL) and Et_3N (140 µL). Then, a solution of CuI (1.6 mg, 8

μmol) in DMF/Et_3N (1:1, 120 μL) was added. The mixture was stirred for 60 h at 50 °C and then filtrated and washed with DMF (3 × 20 mL), EtOH (3 × 20 mL), Et_2O (3 × 20 mL). The product was then dried under vacuum (10-5 mbar) at 55 °C for 15h.

8. EXAMPLE 5 - 1/120 TEMPO+Me SBA-15 $_{scg}$ (HYPSO 12) – Co-gel using $(OEt)_3SiC_3H_6N_3$, $(OEt)_3SiCH_3$ and TEOS at the surface of SBA-15 type structured silica followed by TEMPO radical incorporation via Copper-Catalysed Azide-Alkyne cycloaddition (Cu-AAC).

8.1 PREPARATION OF 1/120_N_3+Me_SBA-15$_{scg}$ MATERIAL. REPRESENTATIVE PROCEDURE.

Figure 1 is a schematic presentation of the materials HYPSO 5 (xx) 1/yy and HYPSO 6, 10, 11 & 12 (xx) 1/yy preparation routes involving two steps: first surface treatment, then the alkyne-azido coupling chemical step to attach the radical.

The dry solid of SBA-15$_A$ (0.3 g, see description in example 7.1) is dispersed in 6 mL of pure dioxane, then 0.42 mL of 2.3 mol.L^{-1} HCl solution is added. The solution is then heated in a closed vessel to 70°C. A solution (2.7 mL) containing Triethoxy Azidopropyl silane (0.2 mg, 41 μmol), Triethoxy methyl silane (89.3 mg, 501 μmol) and TEOS (26.1 mg, 125 μmol), and 2.6 mL of clean dioxane is added dropwise over a period of 15-20min under stirring. The mixture is then refluxed for about 1 h. The product is then filtered and washed consecutively with 20/80 water/EtOH (3 × 20 mL), EtOH (3 × 20 mL), and Et_2O (3 × 20 mL), and dried at 135 °C under vacuum (10–5 mbar) for 12 h led to **1/120_N_3+Me_SBA-15$_{scg}$** (ca. 1 g) as a white solid.

8.2 Preparation of 1/120_TEMPO+Me_SBA-15$_{scg}$ (HYPSO 12) through Cu(I)-catalyzed azide-alkyne cycloaddition (Cu-AAC) - Representative procedure

Under an argon atmosphere, O-propargyl TEMPO (25.9 mg, 0.041 mmol) was added to a suspension of **1/120_N$_3$+Me_SBA-15$_{scg}$** (0.3 g, 0.041 mmol azide) in DMF (4.1 mL) and Et_3N (140 µL). Then, a solution of CuI (1.6 mg, 8 µmol) in DMF/Et_3N (1:1, 120 µL) was added. The mixture was stirred for 60 h at 50 °C and then filtrated and washed with DMF (3 × 20 mL), EtOH (3 × 20 mL), Et_2O (3 × 20 mL). The product was then dried under vacuum (10-5 mbar) at 55 °C for 15h.

9. MATERIAL CHARACTERIZATION

The physic-chemical properties of the materials were analyzed by means of N_2-adsorption desorption, TEM and EPR.

Table 1 - Textural characteristics of the materials obtained by N_2-adsorption desorption at 77K.

Materials	Surface Area BET (m^2/g)	Pore volume (P/P_0<0,99) (cm^3/g)	Mean pore diameter d_p BJH (nm)[a]
HYPSO 2 (53) 1/140	856	1,09	8,1
HYPSO 2 (94) 1/100	866	1,15	9,2
HYPSO 2 (115) 1/60	767	1,02	8,0
HYPSO 5 (26) 1/420	247	1,44	28
HYPSO 5 (53) 1/284	254	1,46	28
HYPSO 5 (80) 1/157	250	1,45	28
HYPSO 5 (122) 1/104	254	1,46	28
HYPSO 6 (45) 1/320	256	1,46	28
HYPSO 6 (95) 1/150	254	1,46	28
HYPSO 6 (178) 1/80	256	1,44	28
HYPSO 10 (13) 1/606	300	0,54	5,4
HYPSO 10 (16) 1/420	n.d.	n.d.	n.d.
HYPSO 10 (30) 1/251	n.d.	n.d.	n.d.
HYPSO 11 (74) 1/120	665	0,92	8,1
HYPSO 12 (60) 1/120	637	0,95	4-9

a- From adsorption branch

The total pore volume for the material is greater than 0.9 $cm^3.g^{-1}$, with the

exception of HYPSO 10 (see Table 1, it is a matter of starting material choice), which is important for having a quantity of solution to polarize as large as possible. Indeed, the analyte to hyperpolarize, which is in solution, is impregnated in the dry material using incipient wetness impregnation, i.e. the quantity of solution added to the material is close to the pore volume but smaller than it. It should be noted that the surface area is rather large (>ca. 250m^2/g). This is again, a matter of choice of starting material.

The TEM pictures in **Figure 2** indicate that HYPSO 5 (26) 1/420 presents no structuration at all, while HYPSO 2 (53) 1/140 presents a hexagonal structuration. No modification of the solid morphology before and after the grafting was observed.

Table 2 - EPR characteristics of the materials.

Materials	Radical conc. [$\mu mol.g^{-1}$]	Line width [G]
HYPSO 2 (53) 1/140	53	12.1
HYPSO 2 (94) 1/100	94	12,7
HYPSO 2 (115) 1/60	115	13,5
HYPSO 5 (26) 1/420	26	12,1
HYPSO 5 (53) 1/284	53	12,9
HYPSO 5 (80) 1/157	80	13,5
HYPSO 5 (122) 1/104	122	15,1
HYPSO 6 (45) 1/320	45	n.d.
HYPSO 6 (95) 1/150	95	13,9
HYPSO 6 (178) 1/80	178	16,8
HYPSO 10 (13) 1/606	13	n.d.
HYPSO 10 (16) 1/420	16	n.d.
HYPSO 10 (30) 1/251	30	n.d.
HYPSO 11 (74) 1/120	74	12,9
HYPSO 12 (60) 1/120	60	n.d.

According to (Jeschke, G. *ChemPhysChem* **2002**, 3, 927), the average inter-radical distance can be directly probed by the peak-to-peak line width in the

EPR spectra, thanks to the strong electron dipolar coupling and/or spin exchange that leads to broadening of the signal. However, this physical behavior is limited to an inter-radical distance of approximately 2 nm, above which the dipolar coupling vanishes. The EPR linewidth (see Table 2) measured for HYPSO 2 varies from 12.1 to 13.5 G for radical concentration ranging from 53 to 115 µmol g^{-1} (62 to 150 nmol.m^{-2}). The EPR linewidth measured for HYPSO 5 varies from 12.1 to 15.1 G for radical concentration ranging from 53 to 115 µmol g^{-1} and is 13.9 G for HYPSO 6 (95), which higher but comparable to HYPSO 2 results. It should be noted that a distribution of radical per surface area of solid is more realistic for comparing those materials (the difference in surface area between HYPSO 2 and HYPSO 5&6 is important), and the values indicate close values and even lower for HYPSO 5&6 when compared to HYPSO 2. HYPSO 11 presents the same linewidth than HYPSO 2, proving the homogeneity of functionality distribution at the surface of the support using this technique.

The analysis of EPR linewidth indicates that the materials do not present any major heterogeneity of the radical distribution (which would lead to a significant increase in the linewidth), which cannot be anticipated by the man killed in the art, considering the preparation process.

10. DNP EXPERIMENTS - Low temperature D-DNP with direct ^{1}H polarization and ^{13}C polarization by $^{1}H \rightarrow ^{13}C$ CP

Description of the equipment

Low-Temperature D-DNP – Polarization of 1H.

The DNP apparatus is equipped with a DNP insert that comprises a microwave shield coupled to an oversized circular waveguide for microwave irradiation and a doubly resonant NMR Helmholtz coil of 0.5 cm^3 inner volume (^{13}C and ^{1}H at 71.73 and 285.23 MHz, respectively). The main axis of the radiofrequency (rf) coil is parallel to the static field to enable rapid dissolution. An ELVA (VCOM 10/94/400) microwave source operating at fµw = 94 GHz ± 250 MHz up to Pµw = 400 mW is coupled to a VDI doubler (D200) with ~30% power conversion efficiency. The 1H spins are polarized by microwave irradiation (fµw = 188.3 GHz

and Pμw = 100 mW) at T = 1.2 K. The amplitude of the frequency modulation was set to $\Delta\nu_{\mu w}$ = 100 MHz with a modulation frequency f_{mod} = 10 kHz.
Polarization value is calculated by measuring thermal equilibrium at 4.2K.

Low-Temperature D-DNP – Polarization of 13C by $^{1}H \rightarrow ^{13}C$ CP.

The proton polarization P(1H) is boosted by DNP and subsequently transferred by CP from ^{1}H to ^{13}C. The ^{13}C polarization builds up an iterative CP scheme, comprising two pairs of chirp pulses applied to both ^{1}H and ^{13}C channels with 1-ms duration, 100-kHz sweep width, and B1 = 30 kHz rf amplitude. The ^{13}C polarization is monitored by application of 5° nutation pulses every 30 s. Because the rf fields are currently not sufficiently intense to compete with the dipolar interactions among the protons, the CP transfer is not 100% efficient, and therefore, only a fraction of P(^{1}H) is transferred to ^{13}C. To further enhance P(^{13}C), we reiterate the CP step $5 < n < 20$ times at intervals of 180 s.
Polarization value is calculated by measuring thermal equilibrium at 4.2K.

Dissolution.

Dissolution is performed with 5 mL superheated D_2O (T = 450 K and P = 1 MPa). The time sequence for the whole experiment is as follows: dissolution in tdiss = 700 ms, transfer in ttransfer = 5 s, injection in tinject = 3.5 s. At that stage, the solution is readily available for any application (it can be injected in a syringe for in vivo MRI/MRS study or into a NMR tube). Overall, the hyperpolarized is collected 9.2 s after dissolution step is started.

Sample preparation for Dissolution-DNP of ^{13}C-labelled analyte solution

HYPSO 2 (94) 1/100, HYPSO 5 (53) 1/284 and HYPSO 6 (45) 1/320 were tested with a solution of 3 mol.L^{-1} [1-^{13}C]-Acetate solution in D_2O/H_2O (90%/10% vol/vol). This analyte, along with [1-^{13}C]-Pyruvate, is a standard for DNP-MRI studies of human metabolism (A. Flori et al., Contrast Media & Molecular Imaging, 10 (2015) 194).

Typically, 20 to 25 mg of HYPSO was impregnated with the solution so that the volume of solution corresponded to approximatively 95 % of the HYPSO pore volume (determined by N_2 adsorption at 77K, $P/P_0<0.97$) and the sample was cooled down to 1.2 K in the DNP apparatus.

Experimental method, modelization and fitting parameters

In order to evaluate the HYPSO materials in a general and universal manner, the following experiment for ^1H polarization was designed:

1. A solution of 20 vol% H_2O and 80 vol% D_2O is prepared for ^1H polarization study.

2. 20 to 25 mg of HYPSO is impregnated with the solution so that the volume of solution corresponds to 90-100 % of the HYPSO pore volume, determined by N_2 adsorption at 77K, $P/P_0<0.99$ in the case of those examples (mesoporous materials).

3. The resulting impregnated HYPSO material is cooled down to 4.2 K or 1.2 K.

4. DNP is performed at 4.2 K or 1.2 K by microwave irradiation (188.3 GHz, set for negative DNP, and 87.5 mW) in a field of 6.7 T (285.23 MHz for protons). Frequency modulation can be applied or not. When it was applied, the amplitude of the frequency modulation was set to $\Delta\nu_{\mu w}$ = 100 MHz with a modulation frequency f_{mod} = 10 kHz. The used setup is described in the experimental description.

5. The DNP build-up of ^1H spins is measured with 1° nutation angle pulses followed by an acquisition period of 1ms. The resulting free induction decay is Fourier transformed, phased and integrated to obtain a value of ^1H spin for the corresponding acquisition period. This sequence is applied every 5 seconds during at least 250 seconds (up to 1500 seconds for long build up time), thus, obtaining at least 50 values of ^1H spin.

6. The resulting DNP build-up curve is fitted with function defined in function of time (t) as

$$y(t) = P_{max}\left[1 - exp\left(-\frac{t}{\tau_{DNP}}\right)\right]$$

leading to the values P_{max}, and to the polarization build-up time τ_{DNP}. The fit is performed using the asymptotic-symmetry based method, chi-square minimization being the procedure used to minimize the residual sum of square (refer to "Inference in Nonlinear Fitting" guide line of origin lab for more details)

between the experimental points and the calculated values. The ^1H polarization P_{max} hence obtained is used for comparing the materials and hereunder referred as $P(^1H)$. The build-up time τ_{DNP} (seconds) corresponds to time required to reach 63% of polarization, $5\times\tau_{DNP}$ corresponding to 99% of $P_{max} = P(^1H)$.

Results for direct ^1H polarization

The performance of the previously described HYPSO 2 materials was investigated according to the above-mentioned method. The results ($P(^1H)$ at 4.2 K and 1.2 K and build-up time τ_{DNP} at 1.2 K) are reported in Table 3 – Radical concentration' P(1H) at 4.2 K and 1.2 K and build up time τDNP at 1.2 K for HYPSO 2, 5, 6, 10, 11 and 12 performed with frequency modulation. and **Figures 3 & 4.** The raw data (build-up curves) and their monoexponential fit are plotted in **Figure 5** for HYPSO 2 (94), HYPSO 5 (26&53) and HYPSO 6 (45).

HYPSO 11 polarization is found to be the same than HYPSO 2 with equivalent radical concentration, in line with the EPR linewidth results. HYPSO 12, with methyl groups at the surface, gives results comparable but 10% higher than HYPSO 2.

Overall, the data clearly highlight the good polarization performance of HYPSO 5 and 6 at 4.2 K and at 1.2 K, the large extent of efficient radical concentration. The difference in build-up rate between HYPSO 5 and 6 and HYPSO 2 is noticeable, but may reside in the difference in pore structure, size and volume.

The results of HYPSO 10, non-structured materials with 6 nm pore diameter are higher than all HYPSO families ($P(^1H)$=82% reached), in line with the former statement.

Table 3 – Radical concentration, P(^{1}H) at 4.2 K and 1.2 K and build up time τ_{DNP} at 1.2 K for HYPSO 2, 5, 6, 10, 11 and 12 performed with frequency modulation.

Materials	Surface Area BET (m^2/g)	Pore volume (P/P_0<0,99) (cm^3/g)	Mean pore diameter d_p BJH (nm)[a]
HYPSO 2 (53) 1/140	856	1,09	8,1
HYPSO 2 (94) 1/100	866	1,15	9,2
HYPSO 2 (115) 1/60	767	1,02	8,0
HYPSO 5 (26) 1/420	247	1,44	28
HYPSO 5 (53) 1/284	254	1,46	28
HYPSO 5 (80) 1/157	250	1,45	28
HYPSO 5 (122) 1/104	254	1,46	28
HYPSO 6 (45) 1/320	256	1,46	28
HYPSO 6 (95) 1/150	254	1,46	28
HYPSO 6 (178) 1/80	256	1,44	28
HYPSO 10 (13) 1/606	300	0,54	5,4
HYPSO 10 (16) 1/420	n.d.	n.d.	n.d.
HYPSO 10 (30) 1/251	n.d.	n.d.	n.d.
HYPSO 11 (74) 1/120	665	0,92	8,1
HYPSO 12 (60) 1/120	637	0,95	4-9

a- Polarization performed without modulation. For HYPSO 2 at such concentration (>ca. 110nmolR•.m-2), modulation is of no benefit and generally tends to slightly decrease the polarization.

HYPSO 5, 6, 10, 11 and 12 materials according to the invention have a good radical distribution convenient for effective polarization despite the absence of pore structuration. The size of the pores, the structuration and pore shape are found to influence the polarization performance, a non-structured material with pore size between 1 and 25 nm giving the best results. Considering the profile of the polarization variation with radical concentration, one can expect to reach higher polarization levels for HYPSO 5 and 6, while structured HYPSO 2 reached a maximum at ca. P(^{1}H)=50%.

Results for ^{13}C-labelled analyte solution using $^{1}H \rightarrow ^{13}C$ CP D-DNP

Table 4 – Radical concentration, P(^{13}C) at 1.2 K (using cross-polarization) and the corresponding time required to reach the maximum value (t_{Pmax}) for HYPSO 2, 5 & 6.

Materials	Radical conc. [µmol.g^{-1}]	P(^{13}C) at 1,2K [%]	t_{Pmax} at 1,2K [min]
HYPSO 2 (94) 1/100	94	21	35
HYPSO 5 (53) 1/284	53	15	10
HYPSO 6 (45) 1/320	45	17	23

As shown in Table 4 and **Figure 6**, HYPSO 5 and 6 materials exhibit good and comparable ^{13}C polarization levels for acetate with respect to HYPSO 2. It should be noted that both HYPSO 5 & 6 were not tested with the optimum radical concentration. It should be noted as well that polarization of 3M sodium [1-^{13}C]-Acetate typically gives lower P(^{13}C) values than buffered 3M sodium [1-^{13}C]-pyruvate; 21 % versus 33 % respectively for HYPSO 2 (109) 1/100. Those values can be reached with a ready-to-inject solution for *in vivo* MRI applications, and are satisfactory for such application as the minimum polarization P(^{13}C) for [1-^{13}C]-pyruvate that should be used for prostate cancer is 15% (S.J. Nelson et al., Science Translational Medicine, 5 (2013)). Indeed, in their work, Nelson et al. injected for the first time into patients 31 samples which had an average polarization of 17.8% (ranging from 15.9 to 21.1%).

CLAIMS

1 - Process for polarizing ^{1}H, ^{13}C, ^{15}N or another nucleus of an analyte by dissolution dynamic nuclear polarization (D-DNP), said process comprising the successive steps of:

i) providing a liquid sample containing the analyte to be polarized;

ii) impregnating a porous material carrying radicals with the liquid sample containing the analyte,

iii) cooling the impregnated material, at a temperature in the range from 0.5 K to 300 K,

iv) submitting the impregnated material in the cooled state obtained in step iii) to D-DNP conditions to polarize, directly or indirectly, the selected nuclear spin of the analyte,

v) warming the impregnated material obtained after step iv) and passing a solution through the material which will carry the polarized analyte with it,

wherein the material carrying the radicals which is impregnated in step ii) was obtained by incorporating radicals through covalent bonding on an initial existing porous solid, this initial existing porous solid being exclusively inorganic or being a carbon based solid with a content of carbon representing at least 97% of the mass of the initial existing porous solid.

2 - Process according to claim 1 characterized in that the existing porous solid is an inorganic oxide, preferably chosen among silica SiO_2, alumina Al_2O_3, TiO_2 and ZrO_2.

3 - Process according to claim 1 characterized in that the existing porous solid is formed by carbon atoms directly linked to each other, preferably chosen among carbon nanotubes, carbon fibers, carbon whiskers, charcoal and graphite.

4 - Process according to any of claims 1 to 3 characterized in that the incorporation of radicals in the material used in step ii) is carried by grafting on accessible reactive functions present on the initial existing porous solid of:

- either organic molecules including at least one radical,
- or organic molecules including a functionality allowing in one or several additional step(s), the introduction of organic molecules which include at least

one radical ; for instance, such a functionality is selected from halogen atoms and functional groups such as azide, amine, amide, imine, nitrosyl, carboxyl, ketone, aldehyde, phosphine, phosphate, phosphinite, sulfoxide, -NCO, -CN -OH, -SH, and ether.

5 - Process according to claim 4 characterized in that the organic molecules including at least one radical are grafted on the accessible surface of the material by a connecting moiety corresponding or including -**L1**-, -**L2**- or -**L1**-**L2**-, defined from the material to the radical, with **L1** chosen among the following groups in their bivalent forms: C_{1-20} alkyl, C_{1-20} alkenyl, C_{1-20} alkynyl, C_6-C_{24} aryl, C_7-C_{44} alkylaryl, C_7-C_{44} alkenylaryl, C_7-C_{44} alkynylaryl, the said groups being able to contain triazole and tetrazole units and being unsubstituted or substituted with one or more moieties selected from C_{1-10} alkoxy, C_{1-10} alkyl, C_{1-10} aryl, amido, imido, phosphido, nitrido, C_{1-10} alkenyl, C_{1-10} alkynyl, arene, phosphane, sulfonated phosphane, phosphate, phosphinite, arsine, ether, amine, amide, imine, sulfoxide, carboxyl, nitrosyl, pyridine, substituted pyridine, imidazole, substituted imidazole, triazole, tetrazole, pyrazine, substituted pyrazine and thioether ; and **L2** chosen among -O-, -NH-, -N(C_{1-6} alkyl)-, -N(phenyl)-, -N(benzyl)-, -C(O)-, -C(O)O, -OC(O)-, -S-, -SO_2-, -N=N-, -NHC(O)- and -CONH-.

6 - Process according to any of claims 1 to 3 characterized in that the incorporation of radicals in the existing material used in step ii) is carried by a surface sol-gel step involving an organic moiety carrying at least one radical or carrying a functionality allowing, in one or several additional step(s), the introduction of the organic molecules which include at least one radical, leading to the formation of a layer on at least a part of the accessible surface of the initial existing porous solid.

7 - Process according to claim 6 characterized in that the layer is obtained by a sol-gel method involving at least two precursors:

- at least one tetraalkoxysilane, tetrahydroxysilane, alkoxymetal, hydroxymetal, alkoxyhydroxysilane, alkoxyhydroxymetal, silicate or metallate in which the metal is Zr, Ti or Al,

- and at least one organosilane corresponding to a monosilyl or a polysilyl entity, for instance, chosen among the organotrialkoxysilanes, organotrichlorosilanes, organotris(methallyl)silanes, organotrihydrogenosilanes, di-organosilane such as diorganodialkoxy or dichlorosilane, or disilyl compounds of general formula $X_3Si\text{-}R'\text{-}SiX_3$ with X = halogen, alkoxy, hydroxyl, methallyl or hydrogen, R' being any organic moiety, with at least one of the selected organosilane carrying the organic molecule which includes at least one radical or carrying a functionality allowing in one or several additional step(s), the introduction of the organic molecules which include at least one radical.

8 - Process according to claim 6 or 7 characterized in that the layer is formed:

- either by Si atoms, or Si atoms and metal atoms, linked to each other by linking arms consisting in an oxy bridge and by organic linking arms, with at least some of these organic linking arms comprising one said organic molecule which includes at least one radical,

- or by Si atoms, or Si atoms and metal atoms, exclusively linked to each other by linking arms consisting in an oxy bridge and wherein the organic molecules which include at least one radical are covalently bonded to one Si atom of the layer.

9 - Process according to any of claims 1 to 8 characterized in that the amount of radicals in the material is in the range of 0.5 to 160 µmol per gram of material, preferentially in the range of 2 to 100 µmol per gram of material.

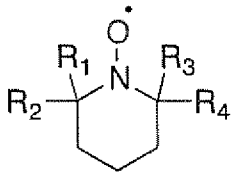
10 - Process according to any of claims 1 to 9 characterized in that the total pore volume of the material ranges from 0.3 to 230 $cm^3.g^{-1}$, preferentially from 0.7 to 150 $cm^3.g^{-1}$.

11 - Process according to any of claims 1 to 10 characterized in that the mean pore diameter of the material belongs to the range from 2 nm to 10 µm, and preferably to the range from 3.5 nm to 2 µm, and preferentially from 3.5 to 500 nm, and more preferentially from 3.5 to 30 nm.

12 - Process according to any of claims 1 to 11 characterized in that the at least one radical is a persistent radical.

13 - Process according to any of claims 1 to 12 characterized in that the at least one radical is chosen among carbon-centered triarylmethyl radicals, nitronylnitroxides, nitroxides such as TEMPO, TEMPOL, azephenylenyls, verdasyls and Fremy's salt, and radicals chosen among perchlorophenylmethyl radical, tris(2,4,6-trichlorophenylmethyl radical), 1,3-bisdiphenylene-2-phenylallyl) and 2,2-diphenyl-1-picrylhydrazyl, galvinoxyl and their derivatives.

14 - Process according to any of claims 1 to 13 characterized in that organic molecules of formula (**A**) including a nitroxyl radical are covalently bonded to the material, with formula (**A**) being :



(**A**)

wherein R_1, R_2, R_3 and R_4, identical or different, are an alkyl (for instance, with 1 to 10 carbon atoms) or aryl group (for instance, with 6 to 12 carbon atoms), substituted or unsubstituted, or R_1 and R_2 and/or R_3 and R_4, as well as R_1 and R_3 and/or R_2 and R_4 are linked together, thus, forming a cycloalkyl, for instance, with 5 to 12 carbon atoms, unsubstituted or substituted, for instance, with one or several phenyl ; preferably R_1=R_2=R_3=R_4=methyl or R_1 and R_2, as well as R_3 and R_4, are linked together and form a cyclohexyl.

15 - Process according to any of claims 1 to 14 characterized in that the initial existing porous solid presents a non-structured porous network.

16 - Process according to any of claims 1 to 14 characterized in that the initial existing porous solid presents a structured porous network, preferably structured in a hexagonal array of the pores or in a cubic or worm-like arrangement of the pores.

17 - Process according to any of claims 1 to 16 characterized in that the material is in the form of a porous powder or of a bulk porous material.

18 - A process according to any of claims 1 to 17 wherein in step iii), the impregnated material is cooled at a temperature in the range of 0.5 K to 15 K, and preferably in the range of 0.5 K to 5 K.

19 - A process according to any of claims 1 to 18 wherein in step v), the impregnated material is warmed by passing the solution through the material.

20 - A process according to any of claims 1 to 19 wherein the impregnation in step ii) is made by incipient wetness impregnation.

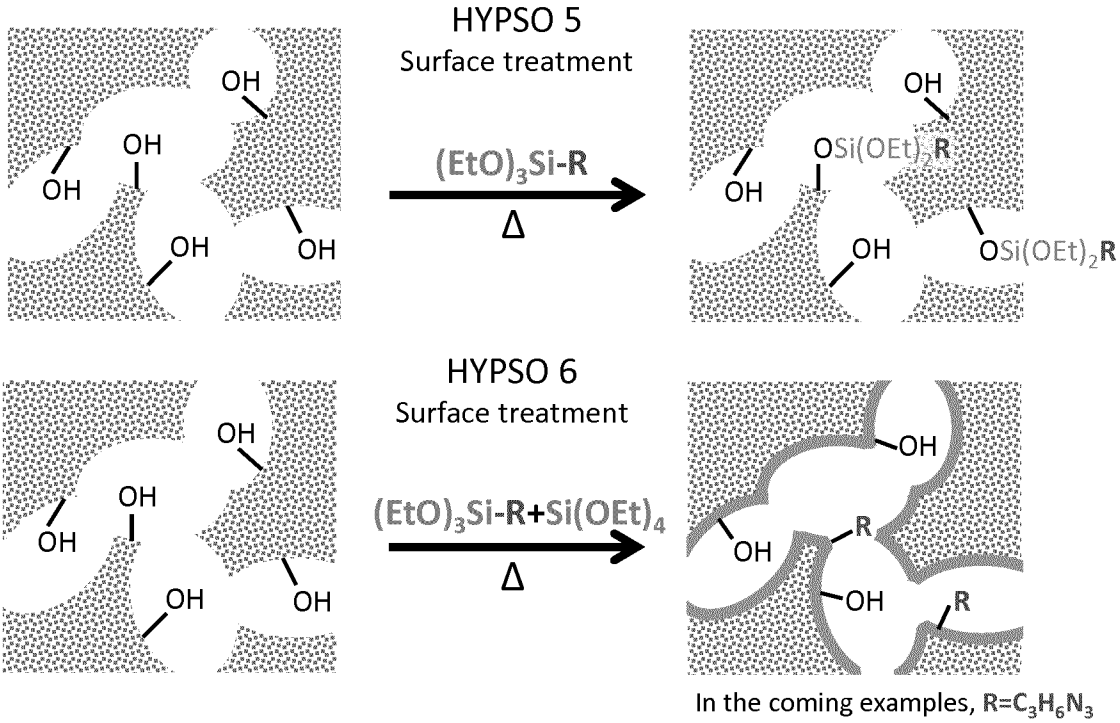
21 - A process according to any of claims 1 to 20 wherein the polarization in step iv) is made by application of a magnetic field and of a microwave irradiation, preferably using a frequency modulation.

22 - A process according to any of claims 1 to 21 for polarizing a nuclear spin other than ^{1}H in which step iv) comprises the polarization of ^{1}H nuclear spins within the analyte by dynamic nuclear polarization (DNP), and the further cross-polarization (CP) from ^{1}H nuclear spins to another nuclei, preferentially ^{13}C or ^{15}N.

23 - Method of analysis by Nuclear Magnetic Resonance (NMR) or Magnetic Resonance Imaging (MRI) of one or more selected nuclear spin of an analyte of interest, wherein the method implements, in a prior step, dissolution dynamic nuclear polarization by a process of any of claims 1 to 22.

24 - Use of a material as defined in anyone of claims 1 to 17 as an electron source for dissolution dynamic nuclear polarization (D-DNP).

Step 1: Surface treatment



Step 2: Chemical coupling

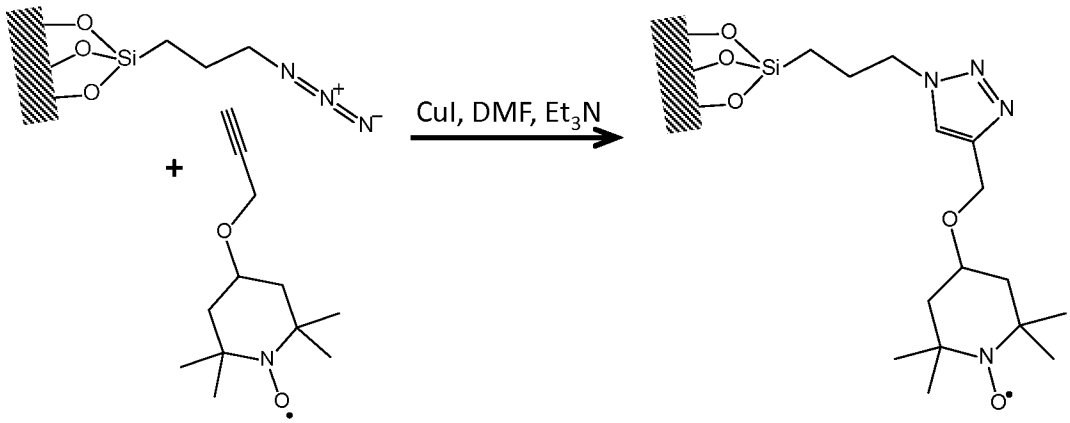


FIGURE 1

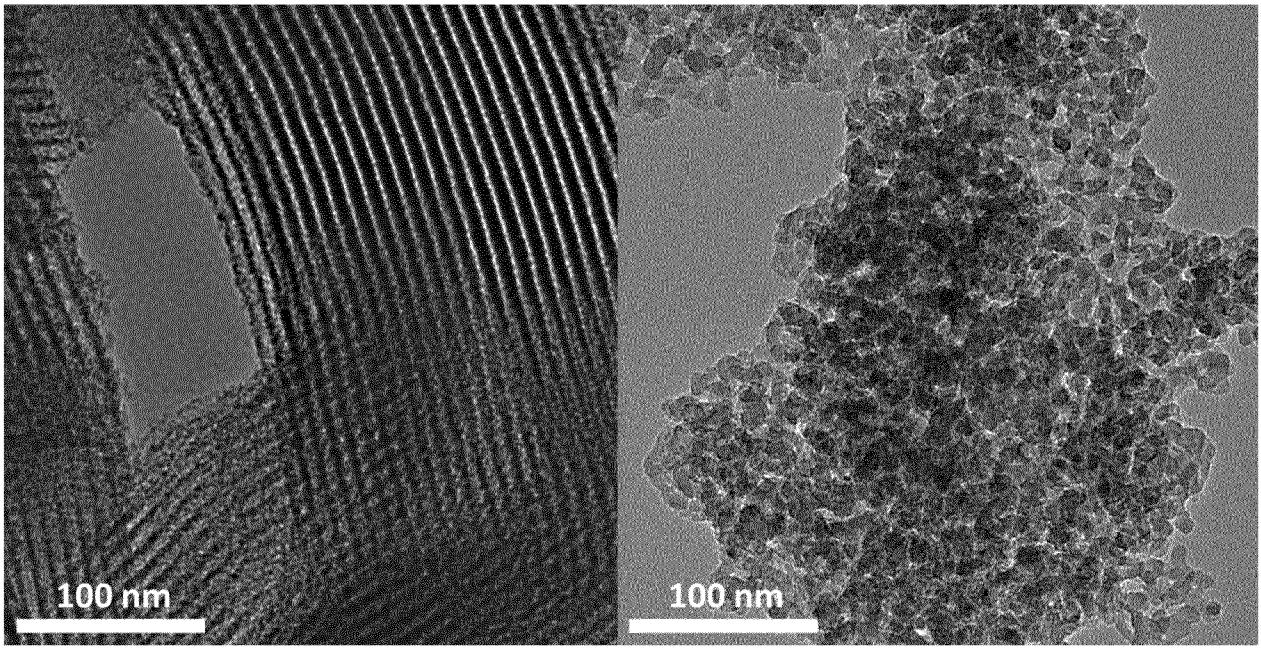


FIGURE 2

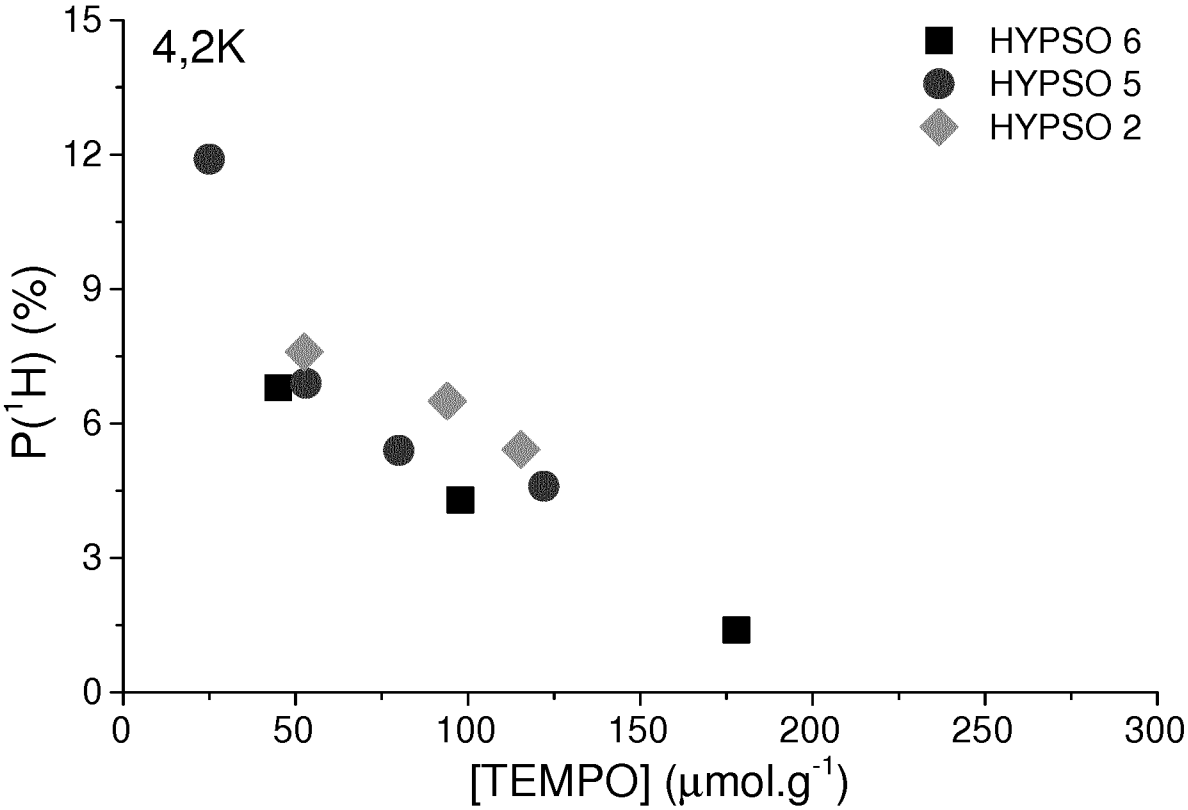

4,2K
HYPSO 6
HYPSO 5
HYPSO 2
P(¹H) (%)
[TEMPO] (µmol.g⁻¹)
0
3
6
9
12
15
0
50
100
150
200
250
300

FIGURE 3

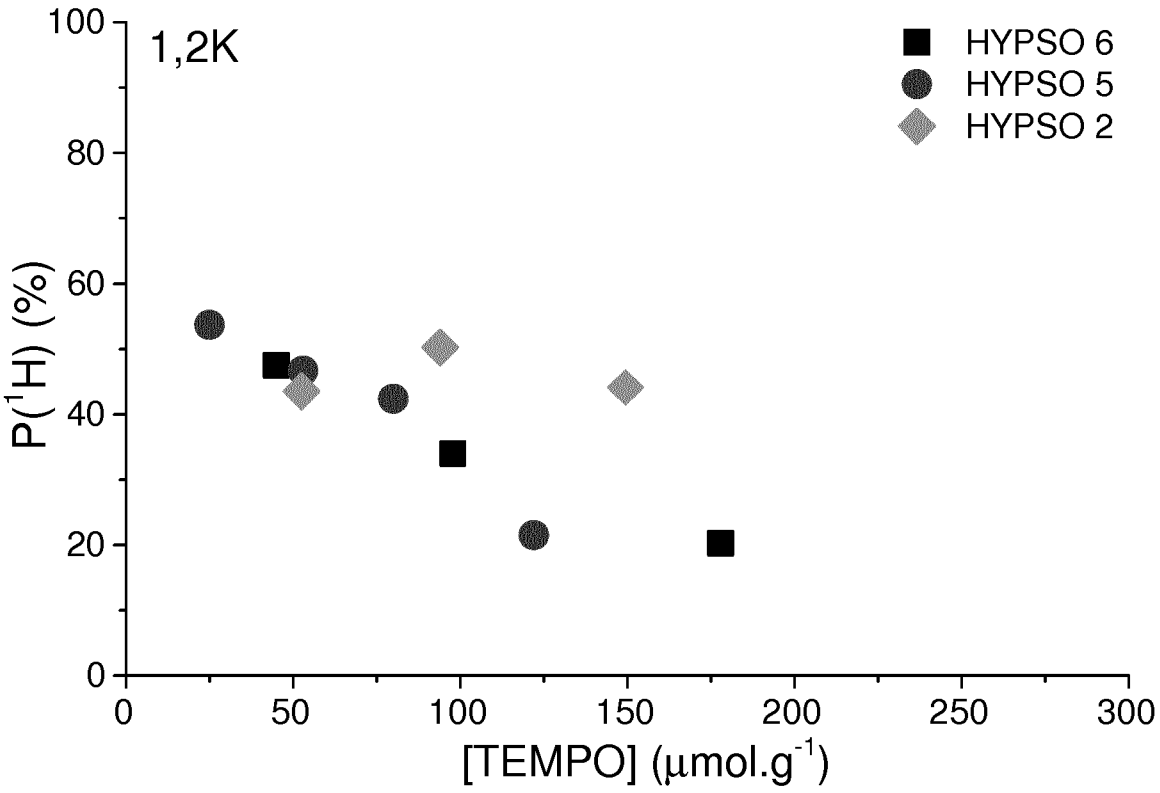

1,2K
HYPSO 6
HYPSO 5
HYPSO 2
P(1H) (%)
[TEMPO] (µmol.g-1)
0
20
40
60
80
100
0
50
100
150
200
250
300

FIGURE 4

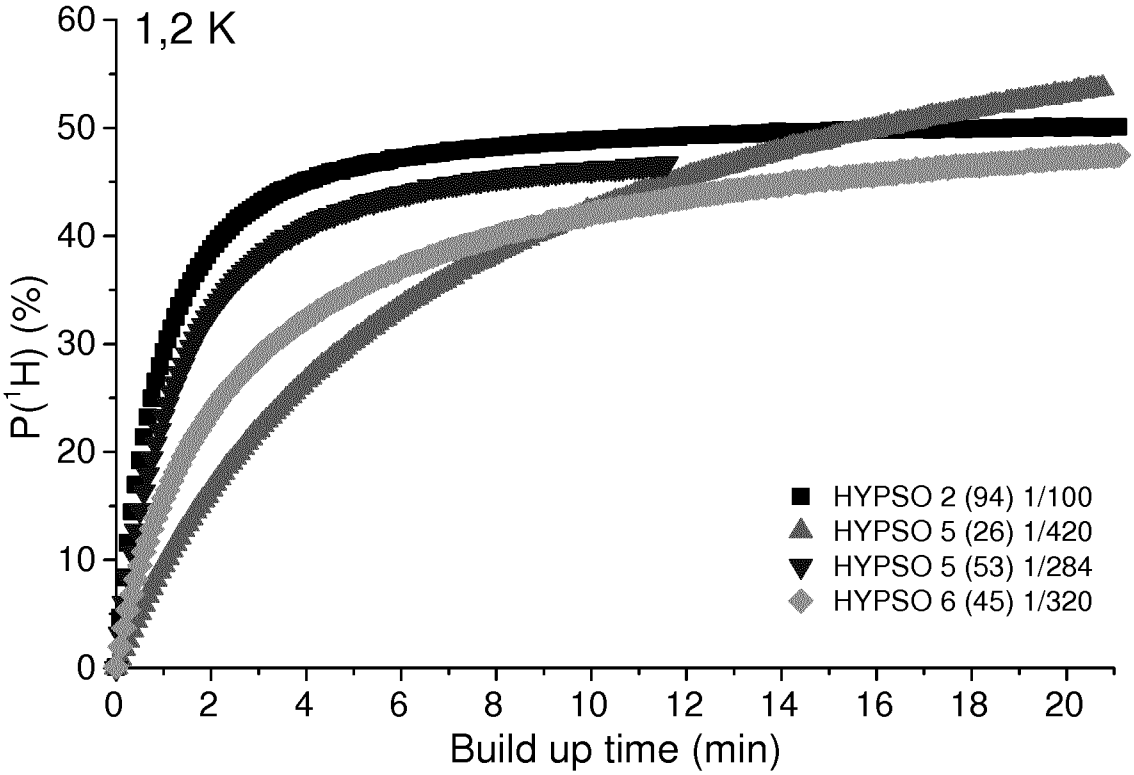

1,2 K
P(1H) (%)
Build up time (min)
HYPSO 2 (94) 1/100
HYPSO 5 (26) 1/420
HYPSO 5 (53) 1/284
HYPSO 6 (45) 1/320
0
10
20
30
40
50
60
0
2
4
6
8
10
12
14
16
18
20

FIGURE 5

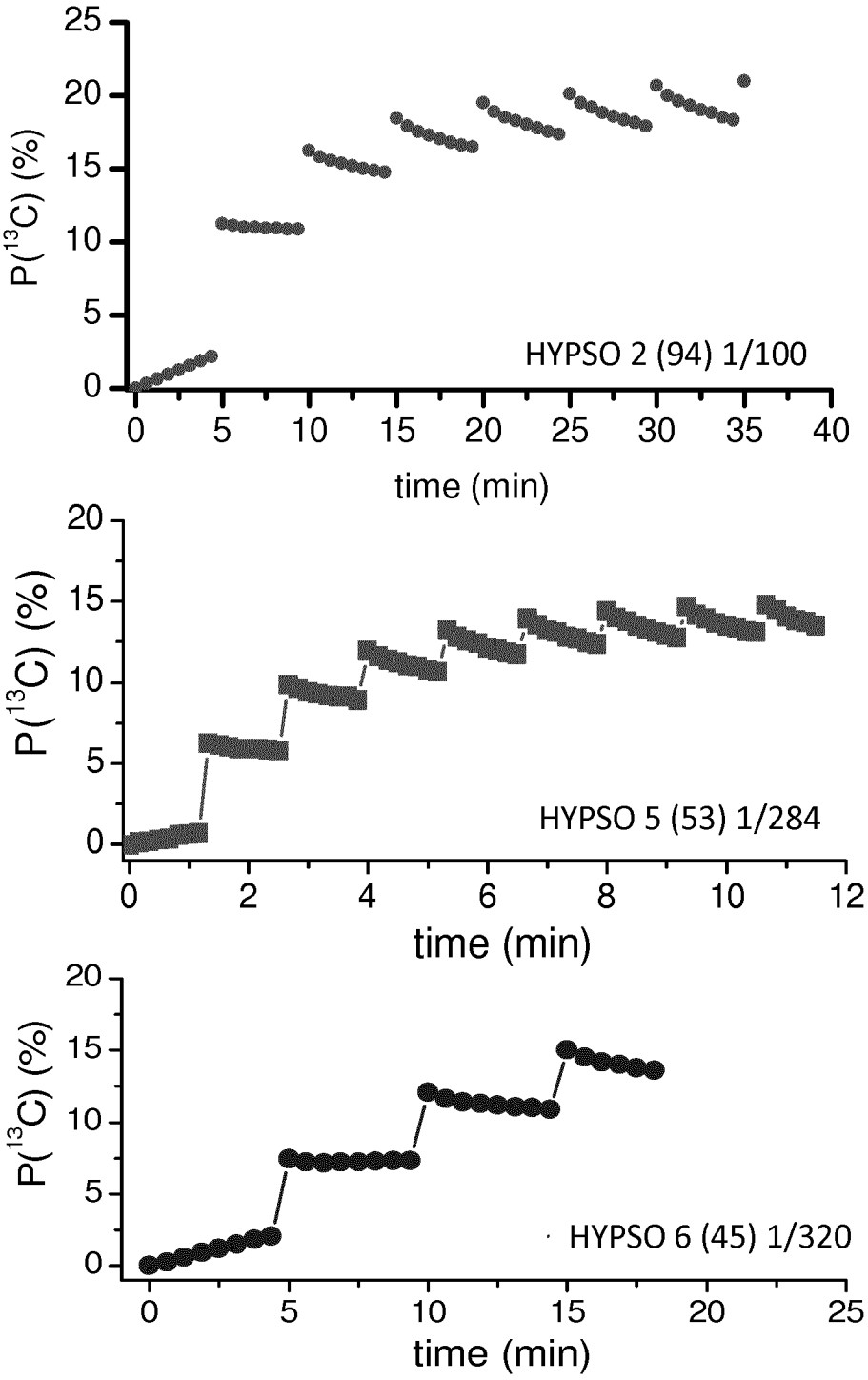


FIGURE 6

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2016/078068

A. CLASSIFICATION OF SUBJECT MATTER
INV. G01R33/28 G01N24/12
ADD. G01R33/62 G01R33/56

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
G01R G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, EMBASE, INSPEC, BIOSIS, COMPENDEX, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	D. GAJAN ET AL: "Hybrid polarizing solids for pure hyperpolarized liquids through dissolution dynamic nuclear polarization", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, vol. 111, no. 41, 29 September 2014 (2014-09-29), pages 14693-14697, XP055204704, ISSN: 0027-8424, DOI: 10.1073/pnas.1407730111 cited in the application the whole document ----- -/--	1,2,4-24

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
1 February 2017	08/02/2017

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Skalla, Jörg

3

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	MCCARNEY ET AL: "Spin-labeled gel for the production of radical-free dynamic nuclear polarization enhanced molecules for NMR spectroscopy and imaging", JOURNAL OF MAGNETIC RESONANCE, ACADEMIC PRESS, ORLANDO, FL, US, vol. 190, no. 2, 19 December 2007 (2007-12-19), pages 307-315, XP022427570, ISSN: 1090-7807, DOI: 10.1016/J.JMR.2007.11.013 figure 1E -----	1,24
Y	US 2015/219734 A1 (GAJAN DAVID [FR] ET AL) 6 August 2015 (2015-08-06) paragraph [0008] - paragraph [0015] paragraphs [0056], [0073] paragraph [0119] - paragraph [0132]; claims 1,4 -----	1,2,4-24
A	AARON J. ROSSINI ET AL: "Dynamic Nuclear Polarization Surface Enhanced NMR Spectroscopy", ACCOUNTS OF CHEMICAL RESEARCH., vol. 46, no. 9, 17 September 2013 (2013-09-17), pages 1942-1951, XP055291484, US ISSN: 0001-4842, DOI: 10.1021/ar300322x the whole document -----	1-24

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2016/078068

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		EP 2880458 A1	10-06-2015
		JP 2015532661 A	12-11-2015
		US 2015219734 A1	06-08-2015
		WO 2014023659 A1	13-02-2014